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THE ROENTGENOGRAPHIC PATHOLOGY OF PULMONARY TUBERCULOSIS

INCLUDING A DESCRIPTION OF TISSUE CHANGES AS REVEALED BY SERIAL STEREOGRAMS AND A CRITICAL STUDY OF THE CLINICAL BEARING OF THE MUTATIONS OF DESTRUCTION AND REPAIR

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INTRODUCTION

The sphere of roentgenoscopy in the diagnosis of pulmonary tuberculosis has been established. It is true that in some quarters faulty technique and unwarranted interpretation still falsely engender doubt and obstruct the wider use of this reasonably dependable diagnostic aid, but experience has defined interpretative standards which to the enlightened are secure. However notable has been our advance in the development of the diagnosis of morbid conditions of the lung by this means, it is equally striking that opportunities for the study of the disease from its inception through all the phases of tissue destruction and repair have been neglected and that the science of roentgenoscopic pathology of pulmonary tuberculosis through comparative inattention has had too slow a growth. For years the clinician's complaint has been that no method at his disposal can accurately trace those finer anatomical and immunological changes that mean so much in treatment and prognosis, while the pathologist laments that at the autopsy table he sees only the end result of the disease. For both the clinician and the pathologist there is an available mode which, if pursued, will yield much if not all of the information sought. By means of serial roentgenograms the mutations of destruction and repair may be depicted at desired intervals for months or years. The evidence is not microscopic; but no other art can ever reveal much of the macroscopic data that this form of biopsy affords. The method has been put to use with great advantage in the study of such acute respiratory infections as pneumonia; but the roentgenologist has lagged in appreciating its applicability in tuberculosis, largely because of the length of time of observation necessary to note the gradual changes. This should not be a hindrance in sanatoria where patients reside for long periods; and the time is at hand when the competent internist must be a master of the roentgenoscopic pathology of the lungs. He must develop the science for its own sake and must be able to interpret tissue changes as clinical fact for, as Waters (1) has recently pointed out, anatomical alterations may precede gross changes in symptoms or physical signs by a considerable time. Various observers, Heise and Sampson (2) among them, have correlated X-ray shadows, physical signs, serological data and symptoms. The contributions have aided materially, but most of them have dealt only with the *status praesens;* and just as the really valuable thing in the therapeusis of tuberculosis is a running clinical record, so sooner or later must be added a serial roentgenoscopic record.

This communication aims to present a brief description of destruction and repair in pulmonary tuberculosis as revealed by serial stereograms, to point out what is typical of each and to designate certain criteria applicable to the interpretation of changing roentgenographic shadows. In addition, it presents a study of groups of cases illustrating destruction and repair, respectively, and using this as a basis attempts to draw certain conclusions as to the clinical bearing of given tissue mutations. The study is the outcome of certain suggestions made by Waters in the paper (1) already referred to.

PART ONE: DESCRIPTION OF TISSUE CHANGE

The roentgenoscopic study of tissue change in pulmonary tuberculosis may well be separated into two general divisions dealing respectively with (1) *destruction* and (2) *repair.*

Under destruction is included the processes of growth of tubercle, or infiltration and caseation, consolidation and cavitation. By repair is meant localization, delimitation, fibrosis, calcification and contraction or obliteration of cavity. In each there are secondary accompaniments and extrapulmonary phenomena to be mentioned, according to their importance. For the sake of completeness restatements of certain well known facts are included; but it is assumed that the fundamentals of diagnosis are familiar. The descriptions concern the ordinary chronic types of disease.

1. DESTRUCTION

a. Infiltration. Active infiltration, which is the beginning of all chronic pulmonary tuberculosis, is usually first observed as a change of the normal trunks and linear markings of the lung field, so that they present what has been described as the "budding twig" or "pussy willow" appearance, most often adjacent to or above the hilum, or as a light, cottony density near the periphery above the third rib. Extending about the latter and leading from it to the hilum may be noted a prolongation, multiplication and fuzzy accentuation of the trunks, a pathological appearance usually accepted as "hypervascularization." At the same time the hilum partakes of the "hypervascularization" and, at times, also of the infiltration, so that, in addition to old, well circumscribed densities, it often partly or entirely loses its original contour and shows a widening, general accentuation, morular nodulation and indefiniteness of outline. Over all there may be a light haziness.

At this point it is well to interject the statement that, in the very early stages of the disease, reliance should not be placed solely on roentgenoscopic diagnosis to the exclusion of clinical observation and repeated physical examinations. The roentgenogram may clearly exhibit the existence of tubercle, but oftentimes only symptomatic and physical data will prove whether this is clinical as well as anatomical. Generally, roentgenoscopic evidence of advancing tubercle signifies clinical activity and serial pictures may be especially valuable at the onset.

Progressing from this incipient stage, the stereogram shows what may be termed in the same figure an efflorescence of the "budding twig," the trunks becoming more accentuated and fuzzy, and the "buds," losing their discreteness and becoming more dense and more like puffs, gradually coalescing with the neighboring shadows. Or the cottony densities may multiply at the periphery and gradually encroach upon the lung toward the hilum until the upper third or half of the field is heavily mottled and the hilum loses its identity in the obscuring shadows. Such mottling may vary from scattered, small fuzzy densities to any degree of confluence of these densities, when it may properly be interpreted as bronchopneumonic or pneumonic consolidation. Dunham's investigations (3) have convinced him that the typical shadow of tuberculous infiltration occurs as a cone, with its apex toward the hilum and its base toward the periphery. Typical mottling has been variously described, but it resembles most closely cirrus clouds which so often break the homogeneity of an otherwise clear sky, and it seems appropriate to designate this appearance as cirrose clouding. If still progressive, this infiltration extends downward and outward from the hilum, while the clouding in the upper third becomes more dense and confluent apace. The mottling of least intensity is in the lower quarter where only a slight fuzzy studding of the descending trunks may be seen. (Series 1, figures 1 and 2.)

The more unusual types of hilum and lower lobe tuberculosis spread, often as a sunburst, from the hilum while the apex remains clear. A pneumonic type, with the axillary triangle, has been described. The mode of progression is from the hilum toward the periphery.

The rate of progression of active infiltration follows no known law and depends on the degree of chronicity of the disease and factors of immunity. The conversion from a few "budding twigs" to general cirrose clouding may occur in a few weeks; usually it requires from several months to a year or more. When it occurs alone, without cavitation, the spread is more rapid and the lung field is often heavily mottled within a space of weeks. The hilum type is also usually more rapid in its extension. In the average case of chronic ulcerative disease the gradual infiltrative change may be detected in serial pictures at monthly intervals.

b. Caseation. There is no definite line of demarcation between the shadow of dense infiltration and that of beginning caseation. Dunham (4) has pointed out that caseation casts the densest shadow next to calcification. So in progressive disease it is to be assumed that the gradual deepening of the density of an area of established consolidation is to be interpreted as caseation. While the periphery of the cirrose cloud widens and coalesces with the adjacent shadows, its centre more nearly approaches opacity and there is established a stage of destruction which is the precursor of encapsulation, calcification or colliquative necrosis. Here again the time intervening between the degeneration of the conglomerate tubercle and the formation of detectable caseation is variable. The transition at its inception cannot be recognized; but it may be said that serial roentgenograms will show change from infiltration to caseation in one month or longer, rarely in a shorter time. In progressive disease the kernel of caseation widens and includes more and more of the cirrose cloud, but the extension of the infiltrative process is more rapid than the spread of caseation. In serial pictures showing no extension of infiltration, caseation may nevertheless gradually replace preëxisting areas of mottling.

c. Cavitation. The rarefaction or excavation of a caseated area can be traced more readily. In two weeks or a month a dense and recognizable shadow of caseation may be seen to gradually melt away. Assuming such an area of cheesy degeneration to be undergoing colliquative necrosis, its centre becomes progressively less dense, it may take on the "bread crumb" or "honeycombed" appearance, or there may be a uniform fading of the centre of the density until the only remaining evidence will be a high light or an area of rarefaction, surrounded by an annular cloud which was formerly the periphery of the caseated kernel. This is the typical ring shadow interpreted as cavity. Where there have been extensive consolidation and caseation, one or more such well defined shadows may appear in a month, or the entire area may become riddled by tiny high lights of rarefaction until its appearance is that of a honeycomb. Many times the process is confined to one lobe, and by a continued rarefaction and merging of ring shadows the entire lobe may become a giant cavity traversed by a network of vessels and fibrous bands which cast quite definite shadows.

In a few instances a ring shadow may extend through what appears to be normal lung tissue without consolidation. The probable reason is that infiltration and necrosis take place simultaneously with little or no collateral inflammation.

In the majority of cases, just as with earlier destructive processes, cavitation proceeds from above downward and its onward march follows a typical course. Assuming cavitation to start at the apex or in the first interspace laterally, two of the more common sites, with consolidation and caseation below it, smaller rings will be seen to form nearer and nearer to the hilum. As they form they merge with the original ring which extends its border inward to the hilum and downward to the interlobar fissure. (Series 2, figures 1 and 2.) In progressive disease this occurs so frequently that the ultimate appearance may often be predicted with accuracy. The total excavation of an upper lobe usually requires a year or more. It must be remembered that the lung may become riddled with cavities in a space of weeks, but this is uncommon and, in the relatively benign and chronic disease as we see it, the destructive process advances slowly over months and years so that its mutations must be followed for a long period of time before the end result is seen.

The roentgenologist may often hazard a guess as to the degree of chronicity or acuteness of the disease from the appearance of the serial pictures. Bushnell (5) writes, "Cavity has been regarded as a sign of immunity but this is true only of the cavity which is encapsulated with fibrous tissue. It is not the presence of a large broken-down focus which constitutes a sign of immunity but the thick, fibrous walls by which said focus has been enclosed." Conversely a large honeycombed, nonlocalized area of caseation means poor immunity, for we know it will almost surely go on to further destruction, while a clean-cut, heavy-walled, well circumscribed cavity that shows no change under the X-ray in a month usually indicates a well established immunity.

It is to be remembered that all destructive changes may proceed simultaneously and that in two pictures taken at a month's interval every phase of destruction may be visualized. It is equally true that destruction must precede repair and that both phenomena, merging one into the other, may often be studied in the same lung field.

2. REPAIR

The initiation and completion of the repair of lung tissue damaged by tuberculosis is much slower than destruction, unless the latter is retarded by the simultaneous development of fibrosis. Repair can also be studied to greater advantage by roentgenography, for the deposit of new tissue and new salts with the secondary mechanical changes can be depicted vividly, whereas the phases of destruction so often can be detected only at their completion and not during the transitional stage. While the autopsy may show in a single specimen every stage of destruction in its proper sequence and inferences may be drawn as to what went before, only serial roentgenograms can reveal whether a given cicatrix represents the site of an obliterated cavity or a healed patch of bronchopneumonia. By no other method can be accurately divined just what vicissitudes of "hypervascularization" and infiltration have preceded the development of the web of scar tissue or how extensive the caseation that has antedated the calcareous deposit. Likewise the time interval can be more accurately gauged. Given a certain picture showing repair, it is often possible to set the minimum age of the lesion.

As an aid in determining the effect of treatment and in making a prognosis, the study of reparative changes in serial pictures is most invaluable; probably more so than a like study of degenerative changes. In point of time and accuracy the method is in many cases far superior to physical examination.

The phases of repair can be arbitrarily and conveniently divided into (a) hilum transformations, (b) clearing, a term of special significance as used here, (c) fibrosis, contraction or obliteration of cavity and (d) calcification.

a. Hilum transformations. These transformations are often striking and in healing disease the differences may be detected within a month. Usually however the transition is gradual and occupies from six months to two years before a permanent picture is established. As noted above, in active, destructive disease there is a hilum that is widened, accentuated, mottled or broken, often studded with puffy, bulging nodules (presumably tubercles or hypertrophied lymph nodes) and usually of an indefinite, hazy or fuzzy outline. The latter is sometimes indiscernible. This appearance, partly or in its entirety, obtains even though the diseased area may be at a distance and near the periphery. As repair ensues it may be noted that within a month's interval the general puffiness subsides and the hilum outline becomes sharper and clear. (Series 5, figures 1 and 2.) Gradually thereafter there is continued contraction of the shadow, and studding and nodulation shrink to smaller dimensions and often become transformed into calcification. Shoots of fibrous tissue may spring from it and the entire structure assumes a compactness that is distinctly in contrast to the surrounding shadows. If such a metamorphosis is observed in a series of pictures where there has been evidence of a previously active lesion, it is safe to assume that the local disease is approaching or has attained the stage of quiescence and chronicity or even permanent arrest. Hilum changes embody a dependable index of the degree of progression or retrogression of the adjacent disease and are subject to prognostic and pathologic interpretations which no pulmonary roentgenologist can afford to ignore.

b. Clearing. This is a term that best describes a certain phase of repair of tuberculous infiltration and applies to transmutations in mottling or cirrose clouding and the surrounding fuzziness of collateral hyperaemia; in short, decongestive changes preceding recognizable fibrosis. (Series 5, figures 1 and 2.) Here again the change may be detected by serial roentgenography within several weeks or a month, although the process may continue over years. At first there is a disappearance of the general haziness and fuzziness, and the mottling and cirrose clouding lose their soft, cottony outlines and begin to exhibit a compactness very similar to that described in hilum changes. Following one of these clouds through a series of pictures, it will be seen to gradually retract its borders, while its centre becomes more dense and its outline more sharply circumscribed. In formerly active lesions becoming quiescent the most striking changes in this direction are noted in the first six to twelve months. During the subsequent years the shadows become smaller and more compact and finally their only remaining vestiges may be irregular, but well defined, stellate densities of varying size—a little studding, a fine stippling—or they may entirely fade out. These mutations are invariable signs of repair and, if there are no cavities and no other complications, they indicate quiescence and healing. In permanently arrested disease the shadows last described are the enduring sequelae of a specific and availing immunity.

There is a special form of clearing which deserves mention. It is the replacement of clouding and mottling by tiny ringlets, apparently representing a confinement of the process to the peribronchiolar stroma. The appearance is relatively uncommon and is observed only in roentgenograms made with perfect technique. The ringlets, having walls up to 1 mm. in thickness, measure from 1 to 5 mm. in diameter, are closely aggregated and are mingled with heavy, well circumscribed studding, a different aspect of the same phenomenon. We have never observed this appearance except where the disease is retrogressive and it may always be interpreted as an accompaniment of repair.

c. Fibrosis. Fibrosis is a phase of repair which can often be studied quite minutely in serial stereograms. It may give rise to several forms of shadows. Often in an apex that has been previously mottled there may be seen the development of homogeneous clouding, a part of which is usually pleural thickening but, when accompanied by clearing and fading of the mottling, may be taken as fibrosis of the diseased area. In extensive lesions the clouding may become general and at places merge into a total opacity denoting diffuse massive fibrosis and pachypleuritis. In such an event there is retraction of the mediastinum, heart and trachea and diaphragm and, lastly, chest wall. A less frequent type of pleural thickening is that which follows the interlobar fissures, giving rise to thin bands seen first at the hilum and following the expected course to the periphery. (Series 1, figure 2.)

Extrapulmonary fibrosis, when not massive, may appear during destruction or repair as diaphragmatic adhesions, manifested in the secondary mechanical effects as a rugosity, roughening, or actual peaking of the leaf of the diaphragm and less often as an obliteration of the phrenicocostal sinus. Pericardial adhesions may be conspicuous as a roughening and obscuration of the normal outline of the cardiac stripe and an obtuseness of one or both cardiophrenic angles. Except in primary pleurisies these effects occur subsequently to intrapulmonary changes and they may be traced from their very start in serial roentgenograms.

The most striking type of intrapulmonary fibrosis is that which springs from the hilum in the form of easily recognizable densities, best seen where the lesion is confined to the upper half of the lung. As the mottling clears and shrinks, the accentuated and multiplied trunks which radiate from the hilum are seen to become thinner, more dense and more clearly cut. This change continues until there remains a reticulum of intertwined, wavy lines radiating from the root. (Series 3, figures 1, 2 and 3.) The lines are heaviest at the hilum and fade out near the periphery; in time these grow more dense and the general network more closely woven until they may form a compact band. Or there may be seen a deepening of the density of the mottling, along with the general clearing, until the shadows become more or less discrete and shrink to mere fibrils with their longer axes radial to the hilum. Another quite typical appearance is the actual sprouting from the hilum of a thin, dense, tendrillar shadow which pushes its way peripherally along the course of one of the trunks or linear markings. A combination of these strands, oftentimes innumerably, may gradually enclose and entangle the shrinking areas of mottling and press them into progressively narrowing confines. (Series 6, figures 1 to 5.) Such transformations are always seen first in the upper third of the field and, when well developed, may be confined to the upper lobe so that the lesion is delimited by a dense band with sharply defined lower border extending from the hilum to the periphery behind the second or third interspace. Concomitantly there is a general retraction of the lesion upward, so that within six months or a year after such a change has started, a band of fibrosis first noticed at the third rib may be seen tucked up behind the second. The result of such retraction, more or less extensive, may sometimes be visualized as a "closed fan." Often the lesion becomes sharply localized above the interlobar fissure.

The fibrous organization of consolidated tissue which does not undergo extensive softening occurs as a slow replacement of the dense cloud by heavy bands extending from hilum to periphery. The fibrosis is diffuse and eventually becomes shrunken and reduced in size. (Series 4, figures 1, 2 and 3.)

Clearing, in addition to representing decongestive changes, may mark the very beginning of fibrous deposit; at least, it is the direct precursor of fibrosis. The latter is slower in its development. Within a month after clearing has started the inchoate tendril of scar tissue may be seen budding from the hilum, but usually two to six months under best conditions elapse before the new deposit can be identified. If the original lesion is well developed serial pictures will show continued and well marked changes during the next year, after which fibrosis is usually fairly dense and not likely to change form so rapidly. Once its maximum density is attained and there is no recrudesence of disease, the markings are permanent. In older persons, in whom as a rule disease is more chronic, fibrosis is usually more gradual and at the same time more dense.

d. Contraction and obliteration of cavities. The rarefaction of caseated areas may sometimes be viewed as a phase of repair, but from the roentgenologist's standpoint this seems more properly a destructive phenomenon and has been described under that head. The cavity, once formed, may also be subject to repair. But the prerequisite of such repair is fibrosis, so that before healing is established one may see a gradual widening of the ring and its fusion with other similar shadows. (Series 6, figures 1 to 5.) Ultimately, if arrest is to occur, the rate of this widening slackens while the wall of the ring becomes more dense and the collateral haziness begins to clear. The annular shadow may remain stationary for months as the surrounding shadows interpreted as fibrosis deepen. Then a contraction of the ring begins, usually equal in all directions but at times irregular. Simultaneously fibrosis increases in compactness, and there is a quite apparent effort at localization of the diseased area. With large cavities the process may be very slow and finally stops but, contrary to the general impression, small and moderate sized cavities may become completely obliterated, in which event the ring shadow is almost always in an upper lobe and solitary. The single ring may be the result of the fusion of two or more smaller rings, but only rarely have we seen the obliteration of a cavity where there were others adjacent. Obliteration is accomplished by a progression of the changes described above until the site of the former cavity is marked only by a small, fibrotic deposit and calcific density, or a heavy clouding of an apex subtended by a "closed fan" springing from the hilum. (Series 7, figures 1, 2 and 3.)

The mechanism of contraction of cavities, it must be emphasized, is secondary to the shrinkage of surrounding fibrous tissue. Where obliteration is noted it is probable that the cavity walls become approximated and adherent. Occasionally closure may be only apparent, for we have observed one case where, after a few months, the cavity reopened but there is good evidence that genuine and permanent obliteration occurs occasionally, though not frequently. Incidentally it is to be said that, but for serial stereograms made over a period of years, this phenomenon would never have been appreciated.

Cavities are relatively slow to contract and disappear and this slowness is one of the points of differentiation between real cavity rings and spurious annular shadows. The time required depends on the factors of size and age of the cavern, amount of fibrosis and general appearance of the lesion. Naturally, the larger the cavity the longer time needed for its obliteration. The largest cavity we have ever seen completely obliterated measured four centimetres in diameter in the roentgenogram and required two years and four months under ideal hygienic conditions for its closure. The older the cavity and the heavier its wall when first observed the more rapidly will it contract. As previously noted, contraction presupposes fibrosis, so that the rate of reduction in size will be more rapid if there is well established and progressive repair (clearing and fibrosis) in other parts of the lung field, including the hilum. The rate of contraction or obliteration is apparently not accelerated by any extraneous means except the routine hygienic treatment or compression of the cavity by pleural effusion or pneumothorax.

e. Calcification. This is not usually a prominent part of the picture of repair. When present it signifies a well established stage of reparation but it is often confined to such small areas that its effectual participation in the healing process is limited. It has been shown pathologically (6) that calcification occurs only in deposits of caseous material, at first as a finely scattered dust of calcium and magnesium salts. As might be expected, therefore, its development is observed in serial roentgenograms as a gradual deepening of densities interpreted as caseation; occasionally it is seen in the midst of fibrous deposits. In childhood calcification is seen most frequently at the hilum, whereas in adults it develops most often at the site of the oldest and most degenerated lesion which is usually in the upper lobes. As a homogeneous, fuzzy density, interpreted as pulmonary or glandular infiltration, clears, becomes better circumscribed and contracts, its centre often gradually grows more nearly impenetrable. The contraction and condensation continue until there remains an opaque nodule with sharply cut borders and standing out in contrast to adjoining shadows. Most often they are spherical but they may be morular, vermiform or irregular and jagged. Frequently solitary, they may appear closely aggregated in the upper lobes though less numerous in the lower part of the field.

The development of calcareous infiltration may be detected in six or eight months after repair has begun but it is usually two years before the metamorphosis of a given area in the adult lung is complete. At the hilum of a child, calcification may become well established in a year. Once the opaque nodule has formed, it remains permanent in its appearance and represents the ultimate stage of repair. Later it may be expelled through an ulcerated bronchus, but the roentgenogram has never demonstrated the absorption of calcific deposits.

Clearing marks the onset of repair and is significant of the predominance of the resistance of the host over the toxicity of the invader. Calcification is a supreme and concentrated effort at repair. Fibrosis is a desideratum, but fibrosis with obliteration of solitary cavity is the *summum bonum* of all repair.

PART TWO: CLINICAL BEARING OF TISSUE MUTATION

In addition to affording a means of studying macroscopic pathological change, serial stereograms are of vast importance from the purely clinical viewpoint, for there is no other single method of equal accuracy capable of informing the clinician of the anatomical mutations underlying a given symptom referable to the pulmonary lesion. The fallibility of physical signs is common knowledge; indeed, there is no one sign that can be accepted as a reliable measure of the extent of improvement or deterioration. The usual observation of symptoms, including gain or loss of body weight, amount of sputum and manifestations of toxaemia, as well as clinical and serological tests, are all prone to be deceptive and only a study of all these data collectively will allow a reasonably close approach to the correct estimate of a patient's progress. Viewing all criteria separately serial roentgenograms transcend most of them in clinical usefulness, are as reliable as any laboratory method in demonstrating tissue change and provide a material aid in the formulation of a prognosis. As previously indicated they are of highest value when they supplement an intelligent clinical study.

To more clearly define the applicability of the method, to demonstrate its high degree of accuracy in its clinical purport, and to indicate what symptoms may be expected with a given roentgenoscopic change a statistical investigation of two groups of cases, studied by serial stereograms, has been made. The first group comprises 100 cases in which two or more stereograms taken at varying intervals displayed progressive destructive changes; the second includes a like number showing repair. The observations involved the study and comparison of 438 stereograms. The selection of cases was at random and solely from the roentgenographic files. The cases were tabulated and subsequently the clinical records were consulted and a notation of symptomatic data made. The roentgenographic technique in all cases was uniform and correct. The criteria of interpretation were those explained in the first section of this paper.

In the first group destructive changes include progressive increase in infiltration and caseation and the formation and extension of ring shadows or areas of rarefaction interpreted as cavitation. According to period of observation the group is divided as follows: 27 cases, one to three months; 25 cases, three to six months; 33 cases, six to twelve months; 13 cases, twelve to twenty-four months; 2 cases, more than twenty-four months. A tabulation of the data compiled is presented in table 1.

An analysis of this table reveals a number of outstanding facts. Ninety-two per cent of the cases showed progressive rarefaction in addition to the increased mottling and cirrose clouding observed in all, indicating that very few cases of pulmonary tuberculosis show an extension of the lesion without cavity formation. This confirms information at hand from other sources. In a substantial number of cases (49) the destructive process was accompanied by demonstrable fibrosis, an evidence of a coincident but unsuccessful attempt at repair.

The cases were about equally divided in the moderately and far advanced groups.

The average period of observation is interesting for its relative shortness and it is indirectly proved that the destructive process is retarded when accompanied by demonstrable fibrosis.

Complications, both tuberculous and nontuberculous, were frequently observed in all types of progressive disease. The inference is that the large incidence of complications is related not so much to the extent or character of the pulmonary lesion but more to evidence of progressive disease.

The constitutional condition improved in 10 and was noticeably worse in only 46 of the series. Body weight was gained in 31 and lost in only 38 cases. These figures emphasize the unreliability of certain clinical data as indications of changes in the local lesion and reaffirm the proved but in many quarters unappreciated fact that weight may be gained while disease advances.

TABLE 1

One hundred cases in which serial stereograms showed progressive destruction

GENERAL CHARACTER OF PROGRESSIVE, DESTRUCTIVE CHANGE	SINGLE TOTALS	AVERAGE PERIOD OF OBSERVATION IN MONTHS	CLASSIFICATION ON ADMISSION*			COMPLICATIONS		CONSTITUTIONAL CONDITION			BODY WEIGHT			AVERAGE DAILY SPUTUM WEIGHT			B. TUBERCULOSIS IN SPUTUM				HEMOPTYSES	
			Incipient	Moderately advanced	Far advanced	Tuberculous	Nontuberculous	Improved	Stationary	Worse	Gained	Stationary	Lost	Increased	Stationary	Decreased	Positive became negative	Negative became positive	Positive, no change	Negative, no change	More than 10 grams	Less than 10 grams
Infiltration......	5	3.2	0	4	1	1	0	1	3	1	1	1	3	1	4	0	0	0	3	2	1	1
Infiltration with fibrosis	3	4.7	0	2	1	2	0	0	1	2	1	0	2	0	2	1	2	0	1	0	0	0
Infiltration and cavitation.....	43	5.6	1	28	14	9	5	5	19	19	16	11	16	29	14	0	0	10	33	0	12	13
Infiltration and cavitation with fibrosis	49	10.2	0	18	31	15	7	4	21	24	13	19	17	32	12	5	1	3	45	0	11	7
Totals........	100	5.9	1	52	47	27	12	10	44	46	31	31	38	62	32	6	3	13	82	2	24	21

*EXPLANATION OF TERMS USED IN TABLES

Classification: National Tuberculosis Association.

Constitutional condition: Indicates manifestations of general toxemia, such as fever, tachycardia, malaise, night sweats, gastric disturbances, etc. Body weight is considered separately.

Body weight: Gained: Increase of more than 1 kgm. Stationary: Not varying more than 1 kgm. Lost: Decrease of more than 1 kgm.

Average daily sputum weight: Increased: Heavier by more than 5 grams. Stationary: Not varying more than 5 grams. Decreased: Lighter by more than 5 grams.

B. tuberculosis in sputum: If single specimens proved negative, three days' specimens were concentrated and examined by the Ellermann and Erlandsen method.

Considering the average daily sputum weights, in 62 cases there was an increase, in 32 no change and in only 6 a decrease. In these 6 demonstrable fibrosis accompanied tissue destruction.

In this series, 95 cases at some time during the period of observation had tubercle bacilli in the sputum. In the three cases showing tubercle bacilli which later disappeared there was evidence of fibrosis. In two cases where the sputum was persistently negative for tubercle bacilli there was no roentgenoscopic evidence of cavitation and in every case with progressive cavitation tubercle bacilli were at some time demonstrable in the sputum.

TABLE 2

One hundred cases in which serial stereograms showed progressive repair

GENERAL CHARACTER OF PROGRESSIVE REPARATIVE CHANGE	SINGLE TOTALS	AVERAGE PERIOD OF OBSERVATION IN MONTHS	CLASSIFICATION ON ADMISSION			CAVITATION PRESENT	COMPLICATIONS		CONSTITUTIONAL CONDITION			BODY WEIGHT			AVERAGE DAILY SPUTUM WEIGHT			B. TUBERCULOSIS IN SPUTUM				HEMOPTYSES	
			Incipient	Moderately advanced	Far advanced		Tuberculous	Nontuberculous	Improved	Stationary	Worse	Gained	Stationary	Lost	Increased	Stationary	Decreased	Positive became negative	Negative became positive	Positive, no change	Negative, no change	More than 10 grams	Less than 10 grams
Clearing......	27	8.7	1	25	1	10	4	3	24	3*	0	21	6†	0	0	7§	20	11	0	10	6	3	3
Clearing with fibrosis.....	28	15.7	0	20	8	8	5	4	28	0	0	26	2‡	0	2	6§	20	15	0	10	3	1	0
Clearing with fibrosis and contraction of cavity....	32	14.5	1	22	9	31	7	3	30	2†	0	28	1	3†‡	0	10	22	12	0	19	1	4	4
Clearing with fibrosis and obliteration of cavity....	13	17.2	0	10	3	13	2	1	13	0	0	13	0	0	0	0	13	13	0	0	0	1	1
Totals......	100	14.0	2	77	21	62	18	11	95	5	0	88	9	3	2	23	75	51	0	39	10	9	8
Cavitation present...			0	45	17		13	7	59	3	0	55	4	3	1	19	42	27	0	32	3	9	5

* Two cases in this group had nontuberculous complications and one a tuberculous complication.

† One case had a tuberculous complication.

‡ One case had a nontuberculous complication.

§ One case had no sputum.

There was more or less blood spitting in 45 cases. Of these the largest percentage was in the series exhibiting progressive infiltration with or without cavitation but not accompanied by demonstrable fibrosis.

In like manner the data gathered in the study of 100 cases showing progressive repair is collated in table 2. According to periods of observation they are divided as follows: 16 cases, one to three months; 20

cases, three to six months; 31 cases, six to twelve months; 19 cases, twelve to twenty-four months; 14 cases, more than twenty-four months.

In this series of cases it is indicated that there is an average interval of six months between the clearing of mottling or cirrose clouding and the beginning of fibrosis. The contraction of cavities was, in point of time, merely a secondary accompaniment of fibrosis, but the obliteration of cavities required an average of more than seventeen months. It should be noted also that clearing, clearing with fibrosis and clearing with fibrosis and contraction of cavity were observed in about the same number of instances but obliteration of cavity was seen less frequently.

In the 13 cases showing complete obliteration of cavity the ring shadow gradually contracted and disappeared, leaving only a scar, more or less dense, at its former site. As said above, in one of these cases the cavity reopened later but in all the others, so far as observed, closure has been permanent.

Most of the repair group were admitted as having moderately advanced disease but a considerable number (21) were in the far advanced stage. In 20 of the latter fibrosis could be demonstrated, probably because repair had started concomitantly with preceding destruction; clinically these would be classed as markedly chronic cases.

Of the 62 cases showing cavitation at the beginning of the investigation, 44 or 71 per cent showed contraction or obliteration of the cavities. In the remaining 18 the cavities were unchanged but 10 of these were not under observation long enough to expect much contraction.

The incidence of complications showed no special relationship to the phases of repair.

In 95 of the cases the constitutional condition improved and in none did it become worse. Of the five cases showing no constitutional improvement four had complications.

Body weight was gained in a majority (88) of the series. Among those who lost weight, complications seem to have played an important part.

The amount of the sputum decreased in 75 cases, including all those in which cavity became obliterated. In 23 cases, many of which showed unchanged cavities, the sputum was stationary and in only 2 did it increase.

Sputa positive for tubercle bacilli became negative in 51 cases (55 per cent), again including all those showing obliteration of cavity. In 10 cases the sputum remained constantly negative for bacilli and in no case did a negative sputum become positive. In 39 the sputum was persistently positive; in almost all of these cavity was present.

It is desired to emphasize that in all cases where cavity became obliterated the sputum decreased in amount and became negative for tubercle bacilli. Of those showing a reduction in the size of cavity, which however remained patent, the sputum decreased in amount in about 70 per cent and positive sputa became negative in 40 per cent.

Table 3 presents a comparison of the factors contained in the two preceding tables and brings to light some rather striking facts. There is a noteworthy contrast in the average periods of observation of the two classes of cases; 5.9 months for those showing destruction and 14 months for those undergoing repair. This is to be expected since many patients with advancing disease soon become too sick for roentgenoscopic observation and since, as has been pointed out, destructive processes are usually more rapid than the reverse.

Considering the clinical status of the patients on admission, more in the moderately advanced group showed repair than destruction, while the ratio of far advanced cases showing destruction to similar types showing repair was more than two to one. This is significant although not a new revelation to the clinician.

In cases exhibiting cavitation many showed healing, but more continued toward deterioration.

Tuberculous complications were half again as frequent in the presence of progressive destruction, but the incidence of nontuberculous complications was about equal in the two series.

Abatement of the symptoms of toxemia (constitutional manifestations) was observed over nine times in the repair group to once in the destruction group.

In the matter of body weights the ratio was not so high because many patients with roentgenoscopic evidence of progressive disease and with no constitutional improvement nevertheless gained weight.

In 23 and 32 per cent, respectively, of the two groups the average daily sputum weight did not vary. Of the remainder almost every case of repair showed decreasing sputum and in almost every case of destruction there was an increase.

In 61 cases of repair the sputum was negative for tubercle bacilli or became so; in 95 cases of destruction it was positive or became so. During repair 51 bacilli-positive sputa became negative as against 3 during destruction; conversely, during repair no negatives became positive, while during destruction 13 negatives became positive.

Hemoptyses occurred three times during destructive changes to once during the reparative process.

TABLE 3

Comparative recapitulation

FACTORS CONSIDERED	DETAILS	PROGRESSIVE DESTRUCTION	PROGRESSIVE REPAIR
Serial stereograms	Number of cases observed	100	100
Average period of observation	Months	5.9	14
Classification on admission	Incipient	1	2
	Moderately advanced	52	77
	Far advanced	47	21
Cavitation	Pre-existing or developing	95	62
Complications	Tuberculous	27	18
	Nontuberculous	12	11
Constitutional condition	Improved	10	95
	Stationary	44	5 (a)
	Worse	46	0
Body weight	Gained	31	88
	Stationary	31	9
	Lost	38	3 (b)
Average daily sputum weight	Increased	62	2
	Stationary	32	23
	Decreased	6	75
Tubercle bacilli in sputum	Positive became negative	3	51
	Positive—no change	82	39
	Negative became positive	13	0
	Negative—no change	2	10
Hemoptyses	More than 10 grams	24	9
	Less than 10 grams	21	5

(a) Three had tuberculous complications; one a nontuberculous complication.
(b) One had a tuberculous complication; one a nontuberculous complication.

SUMMARY AND CONCLUSIONS

A summary of the facts gathered in this study with conclusions that seem justified follows:

In cases exhibiting roentgenoscopic evidence of progressive disease 90 per cent or more will eventually exhibit ring shadows or areas of rarefaction to be interpreted as cavitation.

In about half of the cases showing destruction coincident repair (fibrosis) could be demonstrated.

The rate of destruction is retarded where coincident repair is demonstrable.

Established progressive destruction is, as a rule, more rapid than established progressive repair.

In cases showing repair, clearing, clearing with fibrosis and clearing with fibrosis and contraction of cavity were observed with about equal frequency.

Fibrosis is recognizable, as a rule, about six months after decongestive changes (clearing) have started.

In a small but considerable number of cases there will be seen a complete obliteration of cavitation; in 12 of this series of 13 such cases closure has been permanent.

Complete obliteration of cavitation usually requires a longer time for accomplishment than any other phase of repair except calcification.

Repair is more likely to be initiated if cavitation does not exist.

At the onset of repair, cavitation was demonstrable in 62 of the 100 cases; of these, contraction or obliteration of cavity occurred in 44 instances. Of the 18 cases where no reduction of the size of the cavity was noted, 10 showed no evidence of fibrosis.

In cases showing cavitation preceding the onset of progressive repair, the cavities will be seen to become reduced in size in a majority of instances (75 per cent or more) if kept under observation for fifteen months or more; in a few of these complete obliteration will be noted.

Most cases undergoing repair were placed clinically in the moderately advanced group but a considerable number (21) were far advanced.

This study indicates that most cases of moderately advanced disease will, under sanatorium care, display roentgenoscopic evidence of progressive repair while a majority of far advanced cases will show the reverse. The minorities however are not negligible.

In the presence of progressive destruction the incidence of tuberculous complications will be greater than where repair is seen.

The incidence of nontuberculous complications does not seem to be related to the character of the intrapulmonary tissue change.

In cases showing local destructive changes a few will manifest lessened symptoms of toxemia, but in about 90 per cent the constitutional condition will become decidedly worse or remain stationary.

Constitutional symptoms will improve and body weight will be gained in almost all cases showing repair.

In the few cases of repair manifesting no constitutional improvement or gain in body weight complications seem to be the responsible cause.

Many patients (31 in this group) will gain weight in spite of roentgenoscopic evidence of progressive disease but more (about two-thirds) will record stationary or decreasing body weight. Where there is evidence of progressive parenchymatous infiltration, without cavitation, the patient is most likely to lose weight.

From this study the inference is that body nutrition is not a dependable index of the changes in the pulmonary lesion unless there is progressive loss of weight.

Changes of constitutional symptoms (other than the state of nutrition) follow anatomical mutations more closely; but even here the margin of error is considerable.

In most cases exhibiting destructive alterations the average daily sputum weight will increase; in a smaller percentage (one-third of this series) it will not vary. In a few cases sputum will decrease but not unless there is considerable demonstrable associated fibrosis.

Where progressive parenchymatous infiltration without demonstrable cavitation is noted the average daily sputum weight usually shows no important variation.

In most cases exhibiting reparative changes (75 per cent in this series) the average daily sputum weight will progressively decrease. In a very few there may be an increase and in the remainder there will be no variation. In most cases of this type, showing no decrease in sputum, cavities will be revealed (20 out of 25).

In a majority of instances progressive decrease in sputum signifies local tissue repair while a progressive increase means local destruction. Where the sputum weight does not vary the chances are about equal, with a slightly greater likelihood of local destruction.

Most cases exhibiting destructive changes (82 per cent in this series) will have sputa persistently positive for tubercle bacilli; of the sputa that are bacilli-negative in the beginning, 80 to 90 per cent or more will sooner or later become positive. A very few positives will become negative but not unless there is considerable demonstrable associated fibrosis.

All cases with progressive cavitation should at some time show tubercle bacilli in the sputum.

In 51 cases sputa, positive for tubercle bacilli, became negative during the period of repair; cavity was present at some time in 27 of these but became contracted or obliterated in 25. In 39 cases the sputum was positive for bacilli throughout the period of observation; in 32 of these cavity was present, becoming contracted in 19 but obliterated in none. In 10 cases, only one of which showed cavity, the sputum was persistently negative for acid-fast organisms. Negative sputa should not become positive if progressive repair is observed.

In this study 95 per cent of the cases showing progressive destruction sooner or later had bacilli-positive sputa, as contrasted with 61 per cent of the repair group which sooner or later had negative sputa.

In all cases where complete obliteration of cavitation was observed the constitutional condition improved, body weight was gained, the average daily sputum weight decreased, and the sputum became negative for tubercle bacilli.

Hemoptyses occurred three times during the process of destruction to once during repair; in cases of destruction hemoptyses were more frequent when no associated fibrosis could be demonstrated.

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DESCRIPTION OF FIGURES

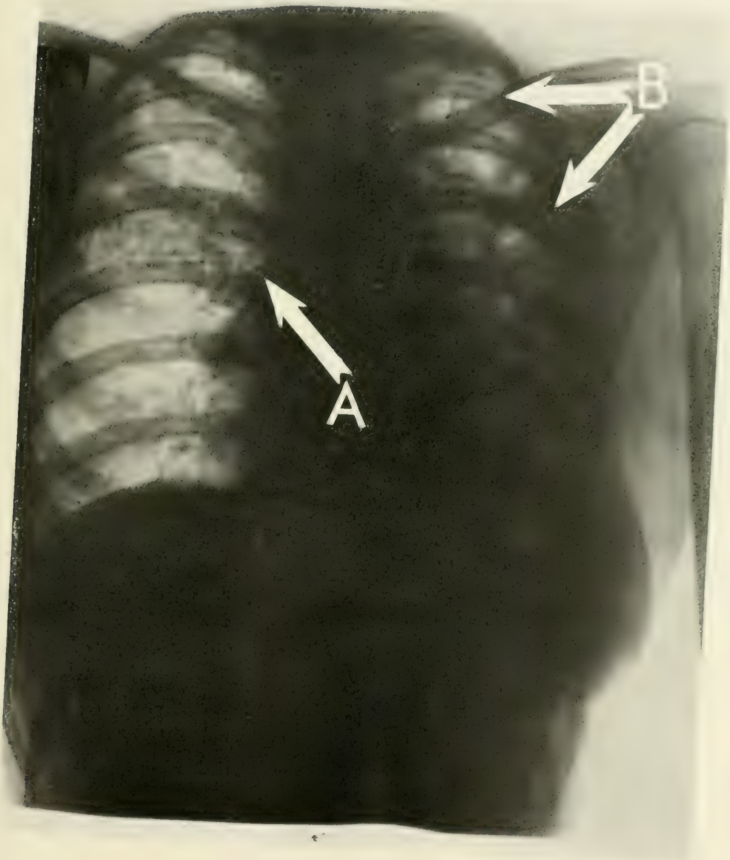
SERIES 1 (PP. 23–24)

Interval between figures 1 and 2, five weeks. Patient aet. 30 on admission; sputum increased in amount and persistently positive for tubercle bacilli; patient died eleven weeks after figure 2 was made.

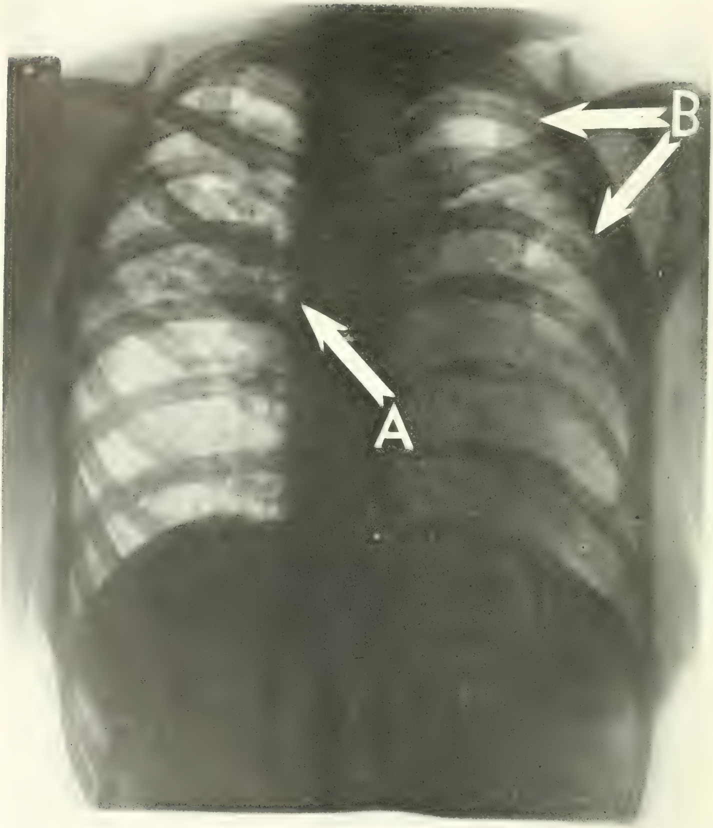
At *A*, in figure 1, is seen moderate mottling and cirrose clouding of the right lung field. In figure 2 this has extended, become more dense and coalescent, denoting the beginning of bronchopneumonic consolidation. In figure 2, in the seventh intercostal space, posteriorly, is seen a sharply defined horizontal line, indicating the development of interlobar pleurisy.

B indicates ring shadows, interpreted as cavities, which in figure 2 have widened, partly merged and extended through the surrounding consolidation and caseation.

Note homogeneous clouding (pachypleuritis) of left lung field with retraction of mediastinal organs and obliteration of phrenicocostal sinus.



SER. 1, FIG. 1



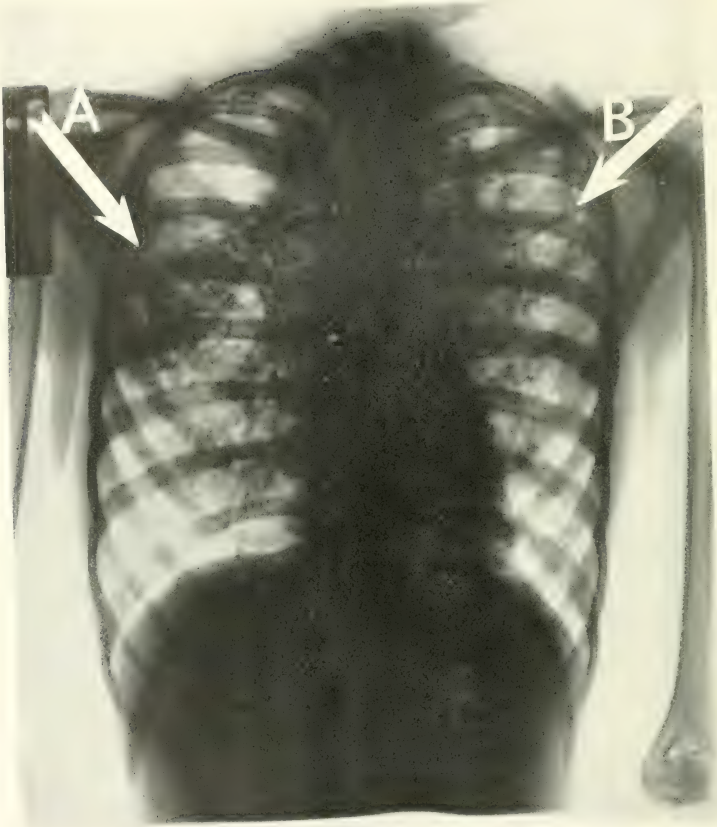
SER. 1, FIG. 2

SERIES 2 (PP. 26-27)

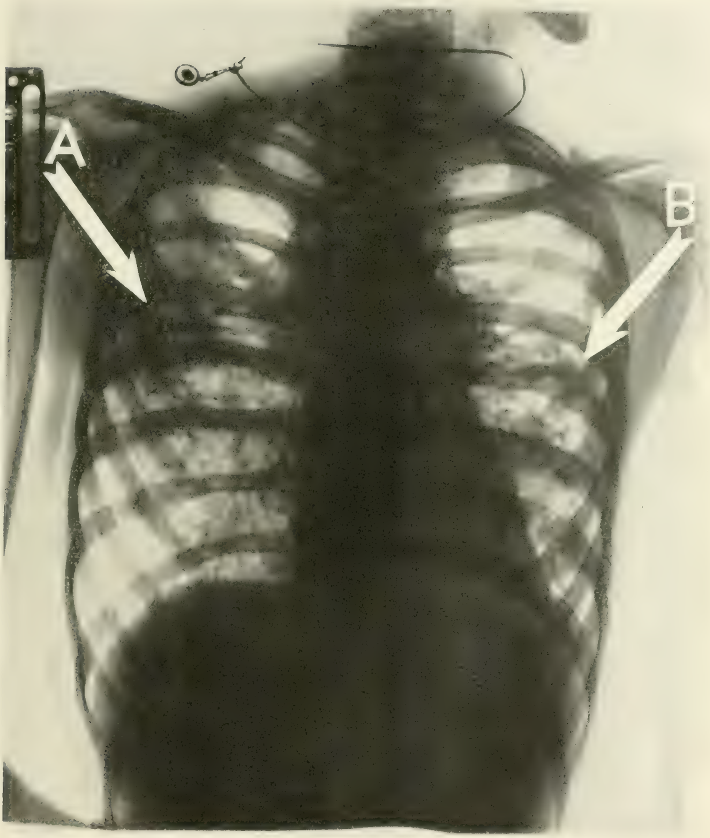
Interval between figures 1 and 2, thirteen and one-half months. Patient aet. 14 on admission; constitutional condition and weight stationary; average daily sputum weight stationary; tubercle bacilli constantly present in sputum.

Figure 1 shows cavitation in both upper lobes, more extensive on the right (lower borders of cavities indicated by arrows *A* and *B*.) Immediately below the large cavities are smaller multiple areas of rarefaction and heavy infiltration; the latter fading out in the lower thirds. In figure 2 is demonstrated the manner in which both upper lobes have become almost entirely excavated. The large rings in figure 1 have merged with the smaller ones immediately below and have extended downward and inward to the hila. Simultaneously the infiltration has caseated and softened and new and small multiple cavities have formed; these in turn will coalesce with the main cavities. This illustrates the typical mode of extension of apical cavities.

Note increasing obtuseness of left cardiophrenic angle and retraction of heart to left, signifying pleural adhesions.



Ser. 2, Fig. 1

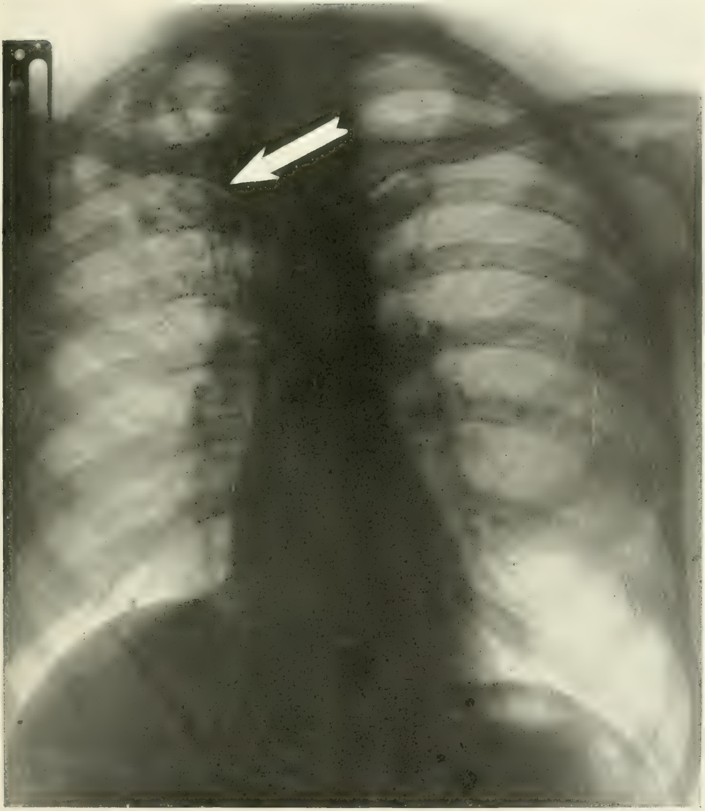


Ser. 2, Fig. 2

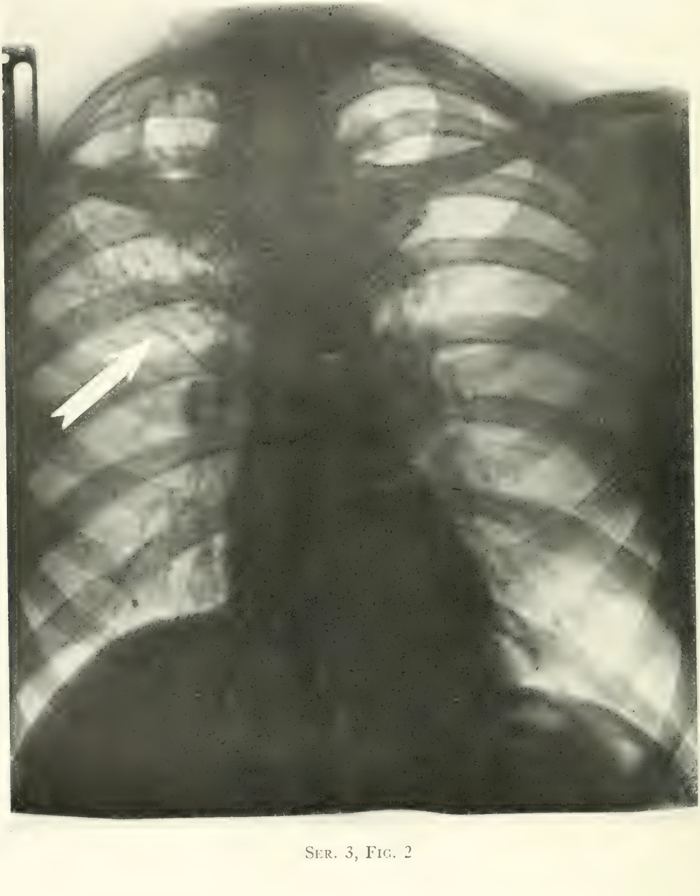
SERIES 3 (PP. 29–31)

Interval between figures 1 and 2, six and one-half months; between figures 2 and 3, three months. Patient aet. 46 on admission; constitutional condition improved and weight gained; sputum decreased but remains positive for tubercle bacilli.

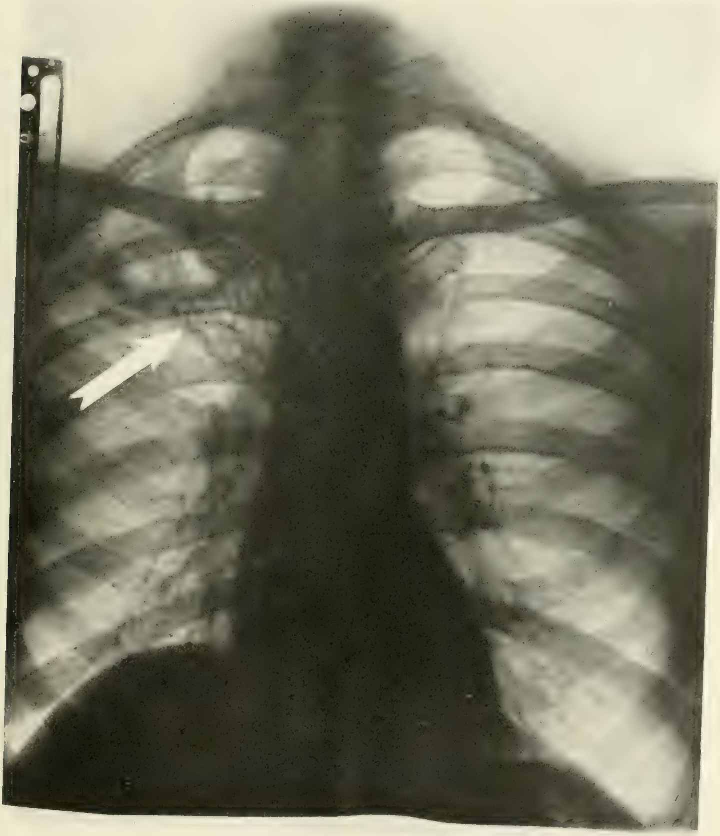
In figure 1 the arrow points to a moderate infiltration of the right lung above the third interspace and seventh vertebral spine, as evidenced by a soft cirrose clouding. Six and a half months later (fig. 2) the appearance has changed and the mottling has been partly replaced by indefinite striations radiating from the hilum to the periphery. In figure 3 these indefinite striations have taken shape as interwoven, wavy lines extending from the hilum, an evidence of beginning fibrosis. Note that the lesion is now fairly well localized above the second interspace and sixth thoracic spine. This illustrates one of the typical phases of repair with clearing and fibrosis.



SER. 3, FIG. 1



SER. 3, FIG. 2

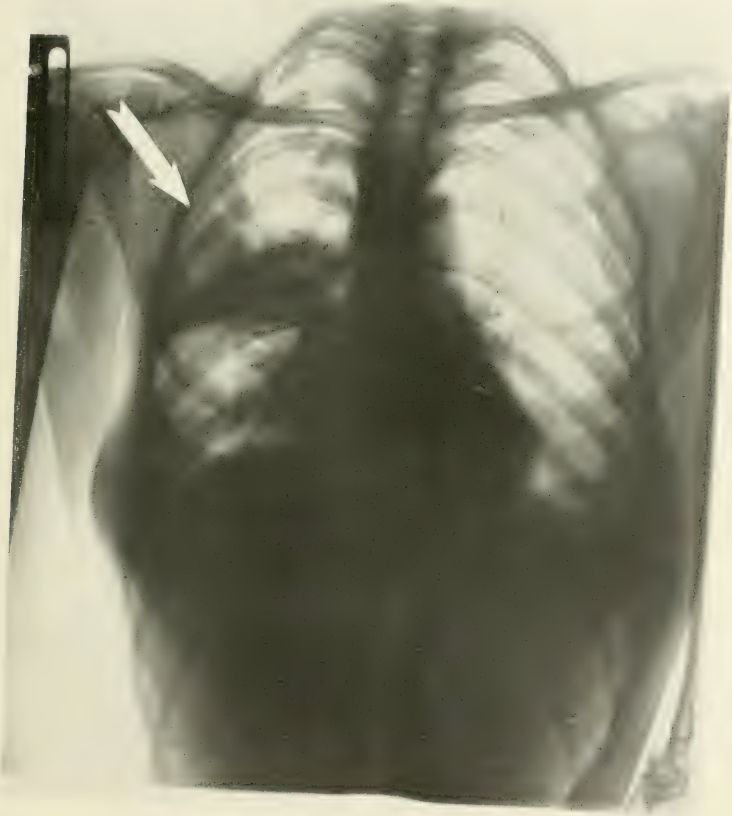


SER. 3, FIG. 3

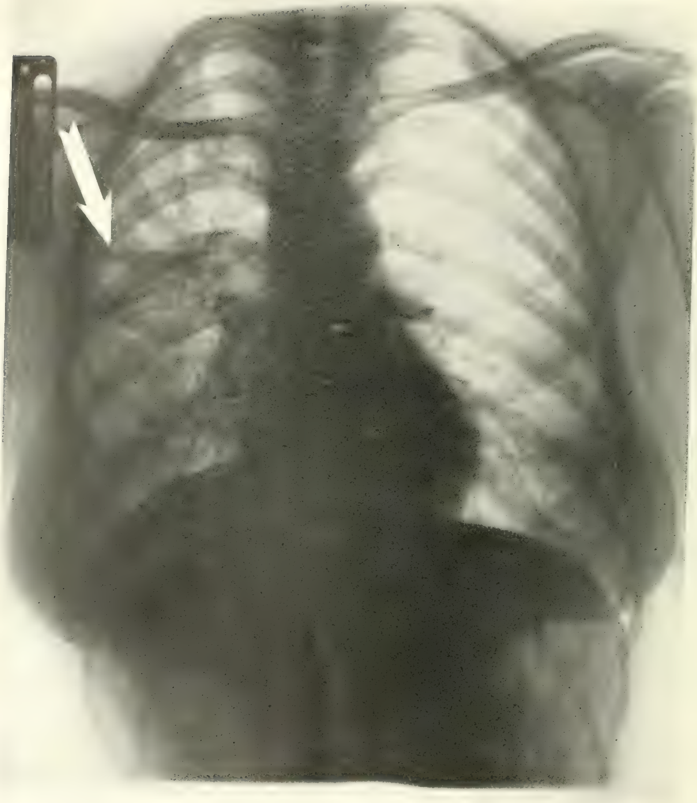
SERIES 4 (PP. 33-35)

Interval between figures 1 and 2, eight months; between figures 2 and 3, four months. Patient aet. 32 on admission; constitutional condition improved and weight gained; sputum decreased; tubercle bacilli, present in sputum on admission, disappeared six months later (two months before fig. 2) and have been absent since then.

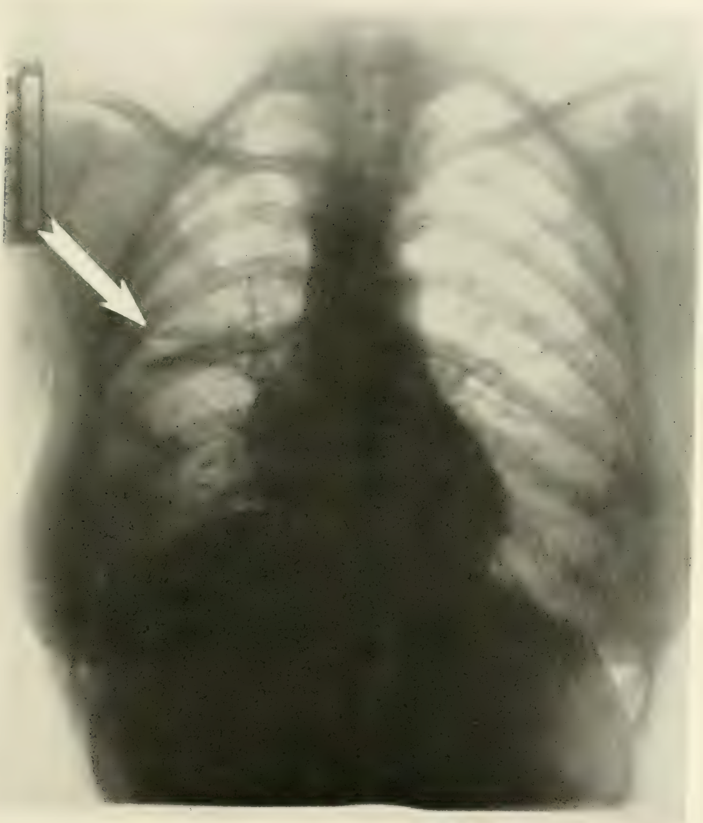
Figure 1 shows an area of consolidation spreading from the hilum into the right lung. Figures 2 and 3 show resolution of the consolidation and replacement by fibrosis. This form of repair is not commonly seen but in this case has accomplished a clinical arrest of the lesion.



SER. 4. FIG. 1



SER. 4, FIG. 2



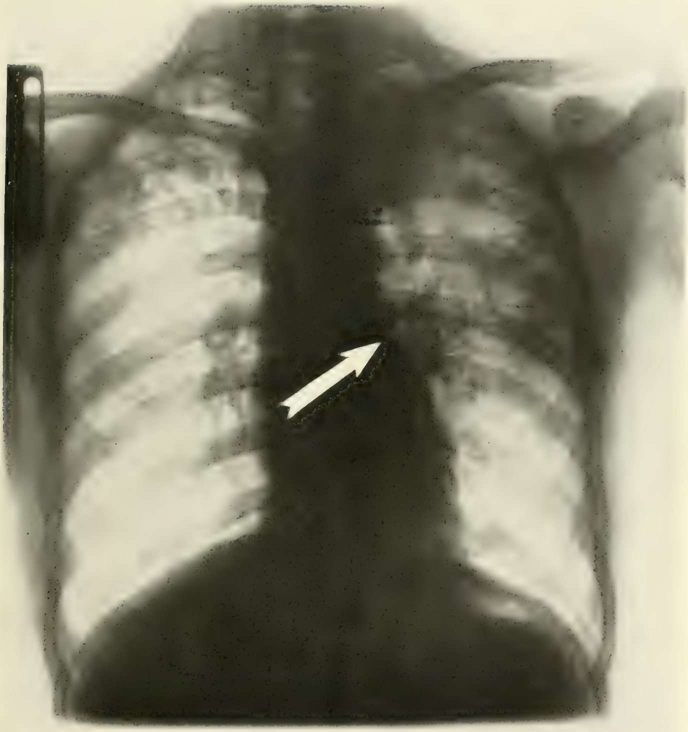
SER. 4, FIG. 3

SERIES 5 (PP. 37-38)

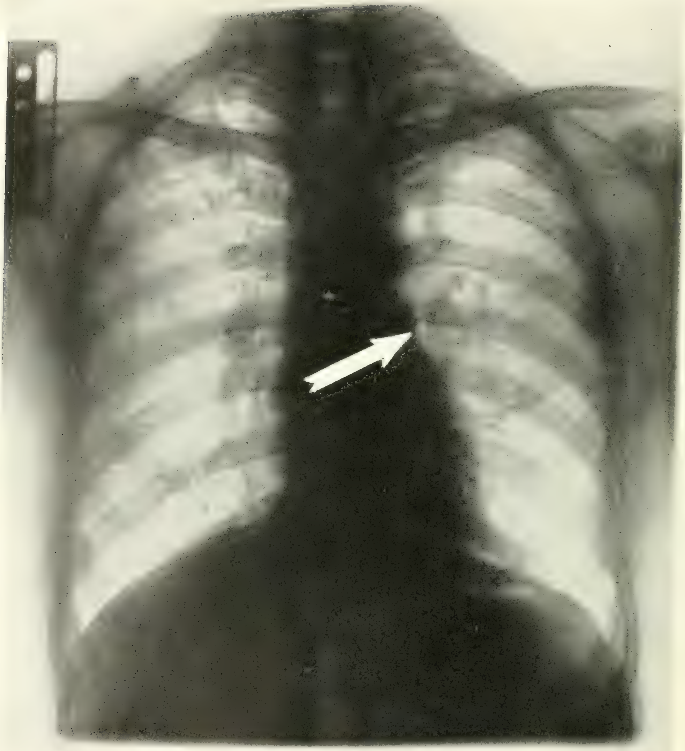
Interval between figures 1 and 2, ten months. Patient aet. 35 on admission; constitutional condition improved and weight gained; sputum decreased in amount; sputum positive for tubercle bacilli on admission; became negative at the time of discharge (fig. 2).

Comparing figure 2 with figure 1, a marked clearing of the cirrose clouding and mottling is noted.

Attention is directed to the left hilum by the arrow. In figure 1 the hilum is accentuated, widened, and the outline is indefinite and fuzzy; in figure 2 it is sharply outlined, stands out in contrast to other parts of the field and has something of its normal contour. Such a hilum transformation invariably signifies reparative change in the adjacent lesion, provided there are no complicating factors.



SER. 5, FIG. 1



Ser. 5, Fig. 2

SERIES 6 (PP. 40–44)

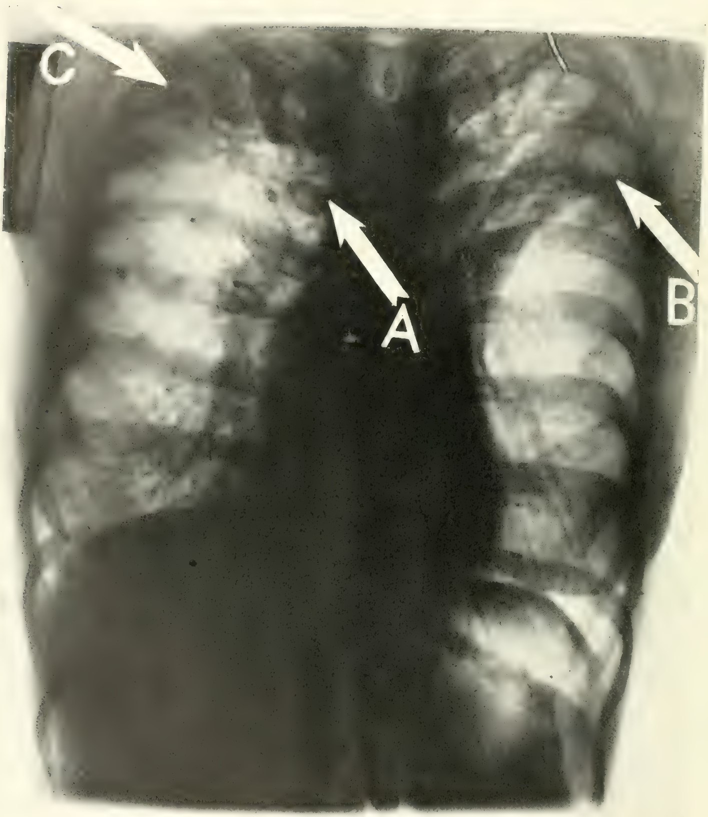
Interval between figures 1 and 2, eight months; between figures 2 and 3, four months; between figures 3 and 4, eight months; between figures 4 and 5, four months. Total period, two years. Patient aet. 48 on admission; constitutional condition improved with occasional febrile exacerbations; weight gained; occasional small hemoptyses; sputum decreased but persistently positive for tubercle bacilli.

Figure 1 shows a relatively old, well localized fibroid lesion of the left upper lobe, with definite cavity at *B* and a more recent, nonlocalized infiltration and consolidation of the right upper lobe. In figure 2, made after a lapse of eight months, the arrow *A* indicates several thin, well defined, tendrillar densities, most marked at the hilum and extending to the periphery behind the second interspace, an evidence of early fibrous deposit. Four months later (fig. 3) these tendrils of scar tissue have become a compact band which, in figures 4 and 5, has become progressively more dense. Coincidentally, the cavity B on the left has contracted until in figure 5 it is almost obliterated.

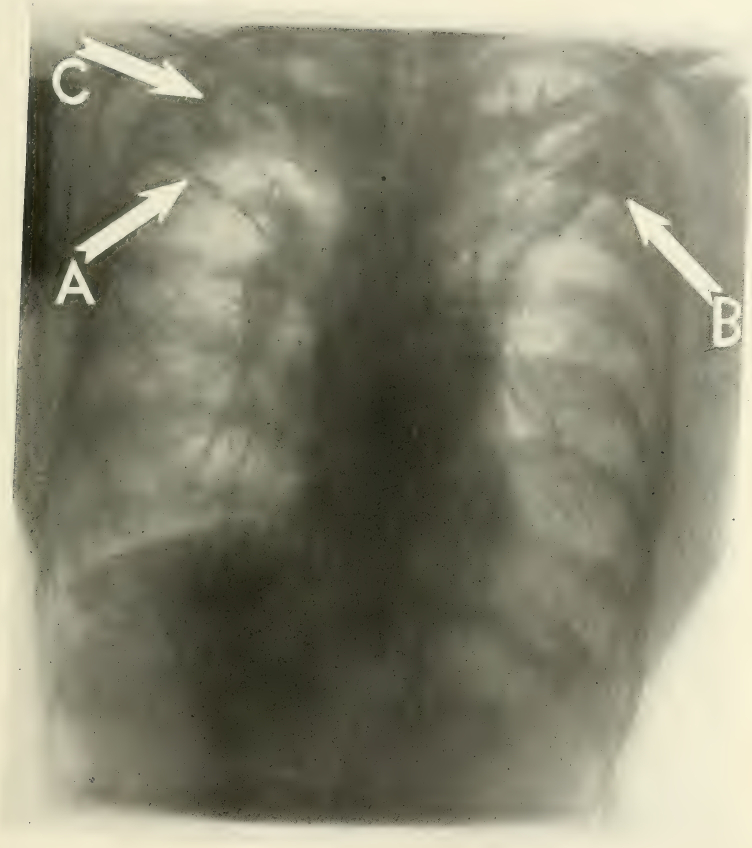
The series illustrates a destructive process as well, for at *C* the area of consolidation in figure 1 has caseated and become partly excavated in figure 2. Tracing the cavity through the remaining figures it is seen to have gradually widened and replaced much of the original consolidation. In due time it is probable that this cavity will contract as did the one in the left upper lobe (B).

Further comparison of the figures shows a general retraction upward of the lesion on each side. On the left the lower border of the density is seen in figure 1 just above the third rib, whereas in figure 5 it is tucked up behind the second rib.

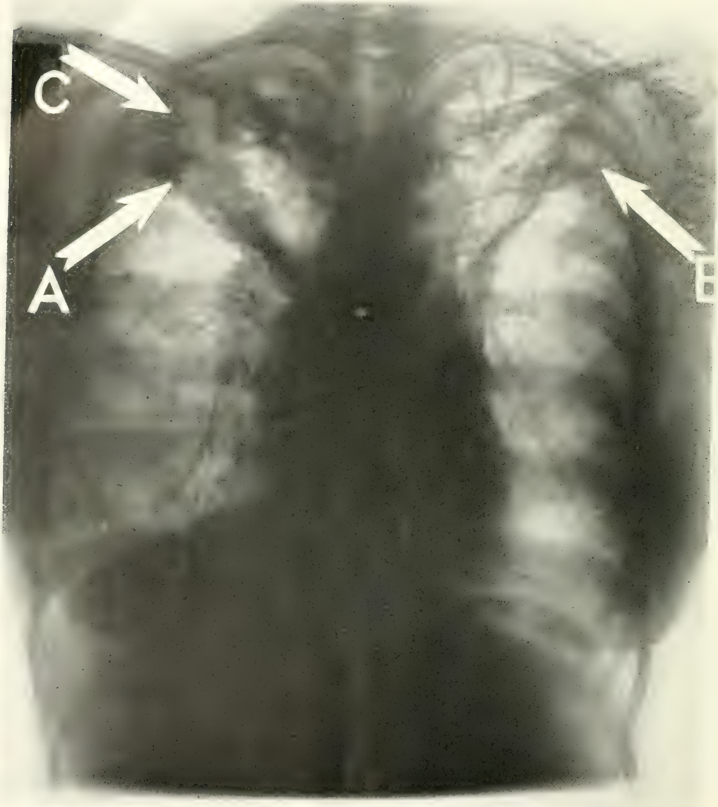
The series demonstrates an effective localization of massive lesions as well as the simultaneous progress of both destruction and repair.



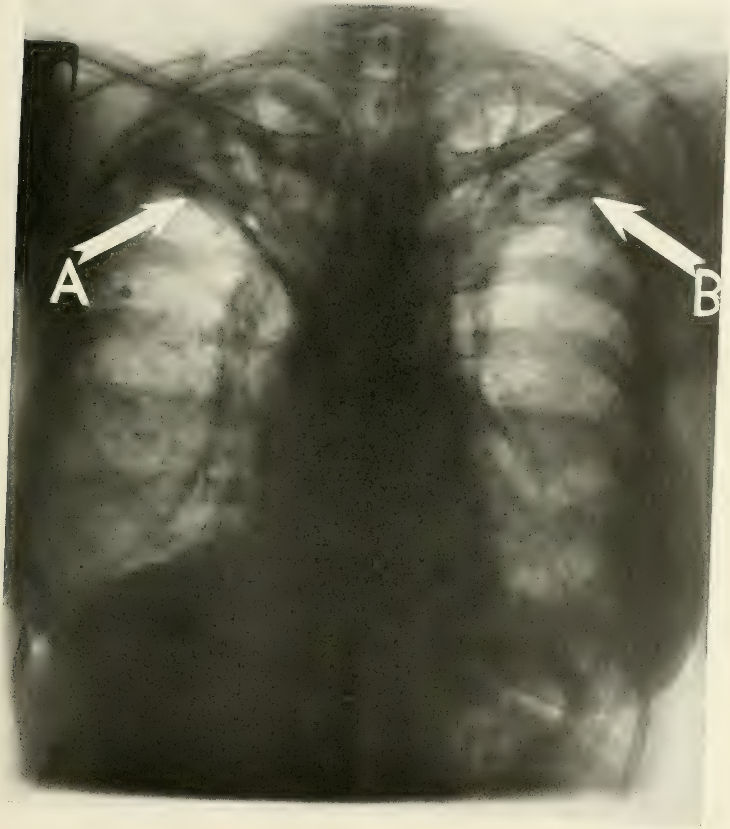
Ser. 6, Fig. 1



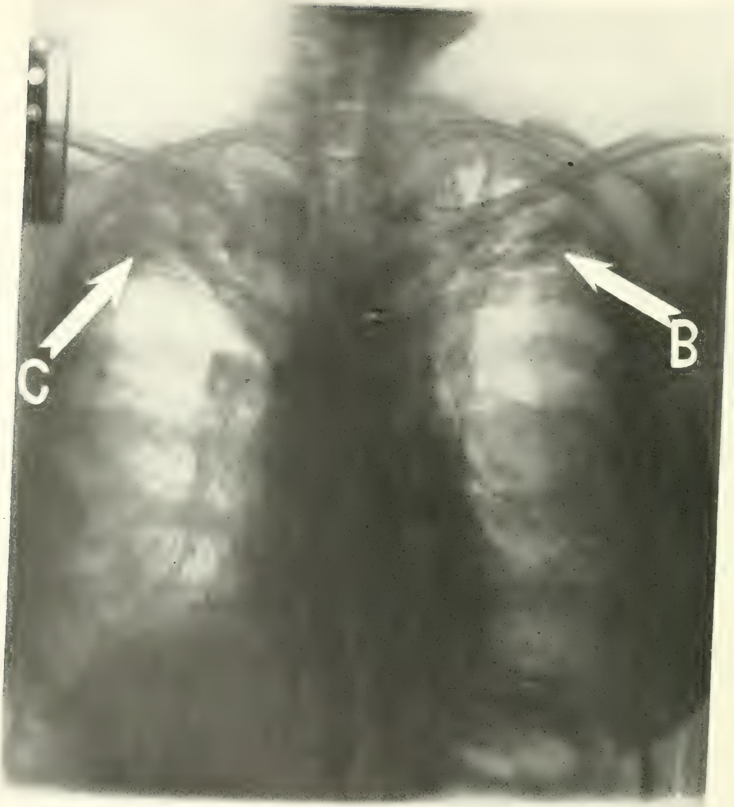
Ser. 6, Fig. 2



SER. 6, FIG. 3



Ser. 6, Fig. 4



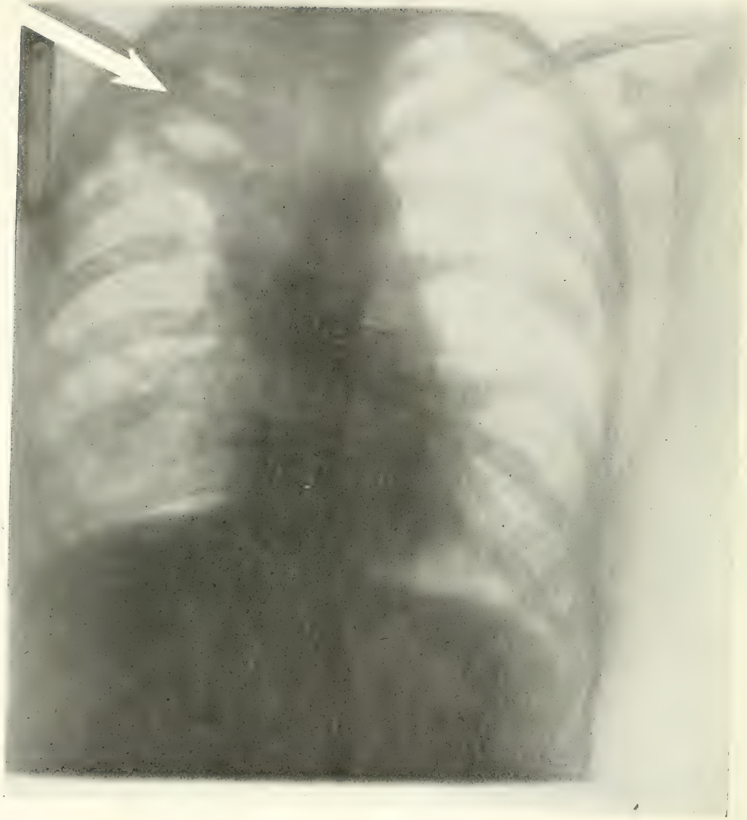
Ser. 6, Fig. 5

SERIES 7 (PP. 46–48)

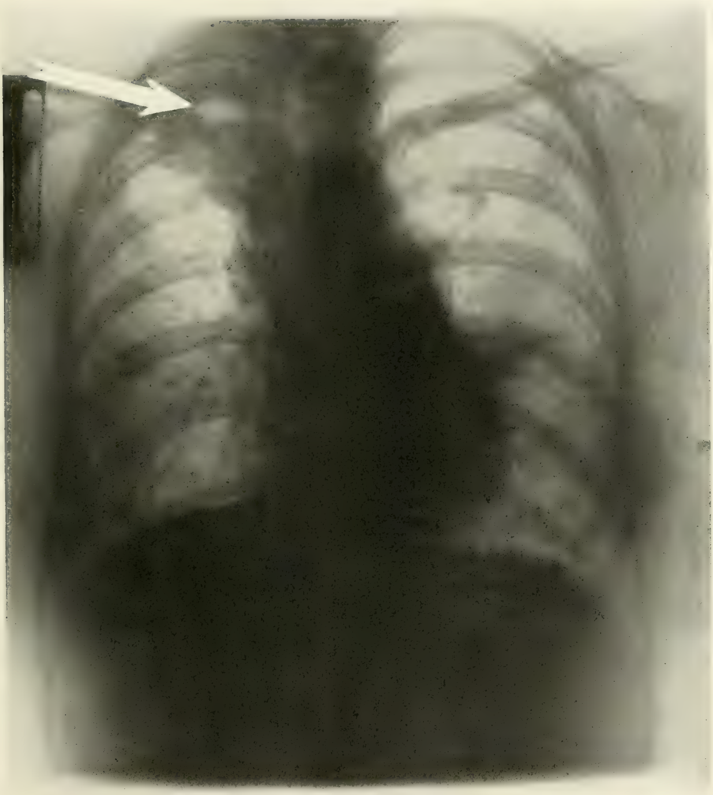
Interval between figures 1 and 2, seven and one-half months; between figures 2 and 3, eighteen months. Patient aet. 34 on admission; constitutional condition improved; weight gained; occasional blood streaked sputum during first year; sputum decreased; sputum positive for tubercle bacilli during first ten months after which it became negative and has remained so.

This series illustrates the closure of a fairly large, solitary cavity indicated by the arrow in the right upper lobe. In figure 1 the lesion is localized above the second rib by a band of fibrosis extending from the hilum to the periphery. In figure 2 there has been a general retraction upward, the fibrosis is more dense and the cavity ring consequently reduced in size. In figure 3 the cavity cannot be seen and all that remains is a diffuse fibrosis of the upper part of the upper lobe.

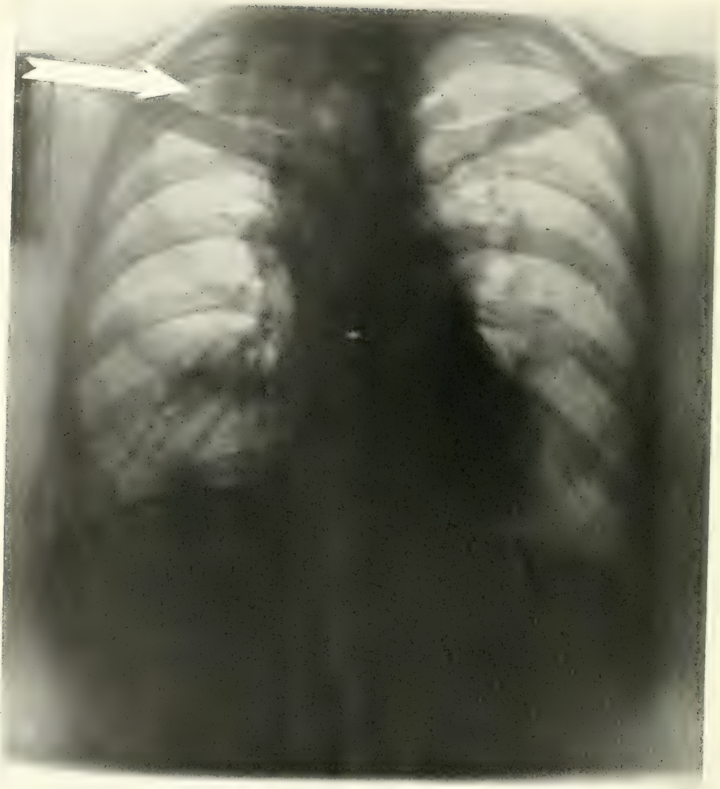
Ring shadows may be masked by overlying fibrosis but, in this case, serial stereograms demonstrated genuine obliteration.



SER. 7, FIG. 1



Ser. 7, Fig. 2



SER. 7, FIG. 3

THE ABSORPTION OF ACACIA FROM THE PLEURAL CAVITY OF NORMAL AND TUBERCULOUS RABBITS

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The mechanism of the production of tuberculous pleural effusions and empyemas is not clearly understood. There therefore remains a great deal of doubt as to just what parts in this mechanism are played by purely mechanical, bacterial or immunological factors. It seems that the majority of tuberculous effusions and empyemas occur mainly in the far advanced cases of pulmonary tuberculosis and in quite a large number of those treated with artificial pneumothorax. To the pathologist it would appear that the predominant parts are played by mechanical influences, such as the necessity for an effusion to fill the space left by an incapacitated lung and subsequent bacterial invasion or contamination occasioning the empyema, or a rupture of the lung with immediate bacterial contamination through the focus of rupture. The immunological factors, however, deserve consideration and it is for this reason that the following investigations were carried on.

That immunological reactions might play an important part was indicated by experiments performed by Paterson (1) in 1917 who found that normal guinea pigs given intrapleural inoculations of tubercle bacilli responded with no noticeable pleural reaction while such injections into tuberculous guinea pigs resulted in the exudation of serum, leucocytes, red blood cells and fibrin. He states that "In attempting to do some experimental work with pleural effusions, it was found that the pleural cavity of rabbits, inoculated with virulent tubercle bacilli after a pneumothorax had been established, did not respond to the inoculation with the development of fluid. It was further discovered that a second inoculation of bacilli into the same pleural cavity some weeks later resulted in a rapid accumulation of bloody serous exudate, rich in leucocytes." He concluded from these experiments that clinical (tuberculous) pleural effusions are caused by the infection of an allergic pleura. Duboff (2), in elaboration of observations by Marshak and Craighead (3), presents a different view of the causation of tuberculous empyemas in man. He believes that tuberculous empyema is a complication of pulmonary tuberculosis, usually the result of lung rupture, that the exudate is pus or seropus in the ordinary sense of the term and that the presence of tubercle bacilli is the rule. Conditions predisposing to lung rupture predispose to empyema, the most potent of these in recent years being induced pneumothorax.

In a previous paper by Corper and Rensch (4), who used rabbits as experimental animals and injected tubercle bacilli suspended in saline-acacia into the pleural cavity, it was found that there was no more tendency to form pleural effusions or empyemas following these intrapleural injections in those animals having received either a subcutaneous or an intravenous injection of the same culture of tubercle bacilli one month prior to the intrapleural injection than in a normal rabbit not having received such preliminary sensitizing injection. Believing that it might be possible to miss finer reactions when using the macroscopic postmortem observations as criteria it seemed desirable to supplement the previous studies by observations on the absorption from the pleura in normal and tuberculous animals of some colloidal substance resembling in many particulars the proteins of pleural effusions.

Crystalloids are unsuited for the study of these conditions, on account of their rapid diffusion from the site of injection and subsequent elimination which has also made them unsuitable for replacing blood in hemorrhage and wound shock. Obviously the use of the serum or plasma of the same animal would not lend itself to satisfactory differential quantitative analysis and the procedure of determining quantitatively the proteins of the serum of another species is beset with difficulties of analysis, besides introducing certain objectionable immunological features. Fortunately, however, recent physiological and pharmacological studies with acacia have placed at our disposal a substance which seemed well suited for our purpose, It can be determined fairly accurately quantitatively as distinct from serum proteins, is not primarily toxic for the animal and does not produce an allergy in itself. In a most comprehensive recent physiological and pharmacological study with acacia Bayliss (5) found that a solution of gum acacia of 6 to 7 per cent in 0.9 per cent sodium chloride solution is capable of effectively replacing blood lost, unless the loss amounts to more than 75 per cent of the blood volume. It has no chemical or drug-like action and can be used in large quantities. Gum acacia does not produce anaphylaxis or hemolysis. The ease of sterilization without disintegration is also a desirable feature of this substance. It is to be preferred over ordinary salt solutions on account of its colloidal nature and the serum protein-like osmotic pressure of its solutions. It resembles the serum proteins in most of its physical properties.

The biological analytical studies with gum acacia or gum saline (a solution of acacia in 0.9 per cent sodium chloride solution) have been made mainly in the application of solutions of acacia for the study of blood volume. Meek and Gasser (6) used acacia for this purpose, giving large amounts intravenously and then analyzing the blood by hydrolyzing the acacia to liberate the pentosan which is determined quantitatively as the phloroglucid. In spite of the tedious technique the accuracy of the method ranged from 76 to 90 per cent recovery of the acacia added to blood. By means of this method they found that after the intravenous injection of acacia solution there still persisted in the blood 77.2 per cent after five hours in one dog, 50 per cent of the original amount injected into another dog after twenty-four hours, while in two other dogs there persisted after forty-eight hours 33 and 42 per cent of the amounts given. McQuarrie and Davis (7) believed the method of Meek and Gasser too time-consuming and preferred the refractometric method of Robertson (8), using the Pulfrich refractometer and determining the acacia in the nonprotein fraction of the blood after precipitating the serum protein with an equal volume of N/25 acetic acid and heat. This method has also a disadvantage in requiring special facilities and an instrument not obtainable in all laboratories, so that it was felt that at a small sacrifice in accuracy which would be balanced by the variations naturally found in different animals a simpler method could be devised for the purpose.

The method finally chosen was to precipitate the serum proteins by the addition of ten volumes of 2.5 per cent trichloracetic acid according to Greenwald (9) in a definite volume (1 cc.) of the fluid to be examined, allowing the mixture to stand for twenty-four hours to insure complete precipitation (four hours was found to be sufficient in preliminary tests), and then centrifugating the mixture at high speed. A definite amount (1 cc.) of the clear supernatant fluid was withdrawn and placed in a Hopkins tube (10), of which the bottom was graduated accurately in 0.01 cc. and readable to approximately 0.001 cc. To this, 10 volumes of chemically pure methyl or ethyl alcohol was added and well shaken. The mixture was allowed to stand at least four hours or overnight and then centrifugated at a uniform high rate of speed (3000 revolutions) for a definite time (ten minutes), after which the volume of precipitate was accurately read. The chemical basis for this method is the complete precipitation of the serum proteins by the trichloracetic acid while the acacia remains in solution, and the final complete precipitation of the acacia by means of the alcohol followed by centrifugation to obtain uniform packing of the precipitate. In order to test the accuracy of this method, known mixtures of dog serum and solutions of acacia were analyzed with the results given in table 1.

TABLE 1

Analysis for acacia in known solutions of various strengths

STRENGTH ACACIA IN SOLUTION	ANALYSIS OF ACACIA IN SALINE SOLUTION. ALCOHOL PRECIPITATE IN 0.1 CC. FLUID	ANALYSIS OF ACACIA IN MIXTURE WITH EQUAL VOLUME OF DOG SERUM	
		Volume of trichloracetic* acid precipitate in 1 cc. original fluid	Volume of acacia† precipitate in 0.1 cc. original fluid
per cent	*cc.*	*cc.*	*cc.*
7.0	0.022†	0.78	0.023
6.0	0.019	0.75	0.017
4.0	0.012	0.70	0.014
2.0	0.006	0.80	0.007
1.0	0.004	0.79	0.003
0.5	0.002	0.79	0.002
0.3	0.001	0.81	0.001
0.1	0.000	0.80	0.000

* One cubic centimetre of fluid was well mixed with 9 cc. of 2.5 per cent trichloracetic acid and after standing at least four hours was centrifugated at a standard speed used throughout this work and the figure is the volume of precipitate (serum proteins) obtained in cubic centimetres.

† One cubic centimetre of the clear supernatant trichloracetic acid mixture (equivalent to 0.1 cc. of the original fluid) was mixed with 10 volumes of alcohol and centrifugated. The figures given are the volumes of the resultant precipitate in cubic centimetres.

An examination of the findings given in table 1 reveals that this method of analysis for acacia in solution in saline solution or serum gives fairly accurate results, sufficiently so to serve the purpose of this investigation.

In order to determine the rate of disappearance of the acacia from the blood, following the intravenous injection of acacia two rabbits (one weighing 7 pounds and the other 8 pounds) were given 50 cc. of 7 per cent acacia saline solution and their blood was examined for acacia, before and at various intervals after the injection for a period of five days. The results of these analyses are given in table 2.

This experiment on rabbits substantiates the findings of Meek and Gasser on dogs, in that intravenously injected acacia persists in the blood of rabbits to the extent that 50 per cent of the original concentration is present after twenty-four hours, while after forty-eight hours 30 to 40 per cent is still present; and within the accuracy of our method it cannot be found to be present five days after injection, indicating that at least 90 per cent of the original concentration in the blood has disappeared before this time.

The following experiments on the pleural absorption of acacia were complicated by a number of factors which made these experiments show a greater individual variation in different animals than that noted in the acacia content of the blood following intravenous injection; and for this reason each experiment of a series included at least five animals in the hope that the average figures from these might give more information than the individual figures.

TABLE 2

The persistence of acacia in the blood of rabbits after intravenous injection

RABBITS	INTERVALS AFTER INJECTION AND RESULTS IN PERCENTAGES										
	Before	Immediately after	2 hours	4 hours	6 hours	10 hours	1 day	2 days	3 days	4 days	5 days
1	0.0	2.2	2.0	1.6	1.7	1.1	1.0	0.5	0.2	0.0	0.0
2	0.0	2.0	1.8	1.8	1.5	1.3	1.2	0.7	0.4	0.2	0.0

There were 37 rabbits included in this series, the purpose of which was to determine whether the absorption of 7 per cent acacia in saline solution was influenced by the previous sensitization of the animals by tubercle bacilli (by either subcutaneous or intravenous injection) or by the presence of tubercle bacilli in the acacia solution itself whether administered intrapleurally to rabbits, either normal or previously sensitized by the subcutaneous or intravenous route. The tubercle bacilli used throughout these experiments was a single strain No. 1851 of virulent human tubercle bacilli. The sensitized animals were given either a subcutaneous injection, 1 mgm., or an intravenous injection of 0.5 mgm. of a good uniform suspension of the bacilli. The animals given the intrapleural injection of the acacia solution plus tubercle bacilli were given 50 cc. of sterile 7 per cent acacia in 0.9 per cent sodium chloride solution plus 3 mgm. of the uniform suspension of tubercle bacilli. The series consisted of 7 control animals given an intrapleural injection of acacia only, 7 rabbits given an intrapleural injection of acacia plus tubercle bacilli, 6 given an intrapleural injection of acacia only four weeks after a subcutaneous injection of tubercle bacilli, 7 given acacia plus tubercle bacilli four weeks after a subcutaneous injection of bacilli, 5 given acacia only four weeks after the intravenous injection of the bacilli and 5 given acacia plus tubercle bacilli four weeks after the intravenous injection of the bacilli. A sample of the pleural fluid was withdrawn aseptically 2 and 6 hours, 1, 2, 3, etc., days after the intrapleural injection. The results of the analyses for acacia (the curve of absorption) are given in table 3.

TABLE 3

The absorption of acacia with and without tubercle bacilli from the pleural cavity of normal and previously sensitized rabbits

PRELIMINARY TREATMENT	INTRAPLEURAL INJECTION	NUMBER OF RABBITS IN SERIES	PER CENT OF ACACIA FOUND IN PLEURAL FLUID WITHDRAWN AFTER					
			2 hours	6 hours	1 day	2 days	3 days	4 days*
Normal	50 cc. 7 per cent acacia-saline	7	7.2†	4.0	1.6	0.7	0.3	Trace
	50 cc. 7 per cent acacia - saline + 3 mgm. tubercle bacilli no. 1851	7	7.0	3.8	2.4	1.0	0.5	Trace
Subcutaneous injection of 2 mgm. tubercle bacilli no. 1851, 4 weeks prior to intrapleural injection	50 cc. 7 per cent acacia-saline	6	6.9	4.2	3.2	1.8	0.7	Trace
	50 cc. 7 per cent acacia - saline + 3 mgm. tubercle bacilli no. 1851	7	6.6	4.2	2.0	1.6	0.3	Negative
Intravenous injection of 0.5 mgm. tubercle bacilli no. 1851 4 weeks prior to intrapleural injection	50 cc. 7 per cent acacia-saline	5	6.8	5.2	3.4	2.0	1.0	0.3
	50 cc. 7 per cent acacia - saline + 3 mgm. tubercle bacilli no. 1851	5	6.8	5.0	3.2	1.0	0.5	Trace

* After the third day it was impossible to obtain fluid from the pleural cavity of more than one-half of the animals and after the fourth day practically none had fluid.

† These figures are the average obtained from all the rabbits in each set from which pleural fluid could be obtained.

An examination of the results recorded in table 3 reveals that the curve of absorption of 7 per cent acacia in saline solution with or without tubercle bacilli from the pleural cavity of rabbits, both normal and previously treated by subcutaneous or the intravenous injection, is, within the limits of the analytical method used for determining this absorption, not appreciably influenced by any of these procedures. It is also worthy of note that the analyses for the serum proteins in the pleural fluid, the results not being of sufficient value to record elaborately, indicated a gradually increased percentage in curve form of these proteins from the time of the intrapleural injection, reaching a maximum in from two to four days and persisting until complete absorption of the pleural fluid had occurred.

SUMMARY AND CONCLUSIONS

With the means applied in this study there was found to be no difference in the absorption of 7 per cent acacia in saline solution, without or containing a suspension of virulent human tubercle bacilli, after intrapleural injection in rabbits both normal or previously sensitized by the subcutaneous or intravenous injection of the same culture of virulent human tubercle bacilli.

This tends to corroborate the previous observation that there is no greater tendency towards the formation of a pleural effusion following the intrapleural injection of a suspension of tubercle bacilli in rabbits which have been previously sensitized with the same culture of bacilli.

There is no evidence in our experiments to prove that in the rabbit tuberculous pleural effusions or empyemas were more prone to form in animals previously sensitized with the same culture of living virulent human tubercle bacilli than in those animals which did not receive a sensitizing injection.

These and previously reported observations do not agree with those of Paterson concerning tuberculous pleural effusions in the rabbit. It is possible that a different reaction may occur in the guinea pig, in view of the generally accepted greater susceptibility of this animal to the allergic reaction. Final judgment on this subject should be reserved pending further observation.

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THE TONSILLAR ROUTE OF INFECTION IN PULMONARY TUBERCULOSIS[1]

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To the somewhat casual reader coming from other specialized fields of medicine, the controversy between the adherents of the inhalation and the ingestion theories of infection by the tubercle bacillus seems as far from solution as ever. Any new data that may be adduced from other fields may therefore be appreciated even though its valuation is difficult or impossible at the present time.

The roentgenologist has frequent occasion to see and note the occurrence of a shadow at the apex of the lung, the significance of which is not entirely clear but is commonly ascribed to a localized thickening of the pleura and is sometimes, for obvious reasons, spoken of as a "pleural cap." Since the study of this condition is scarcely feasible through the medium of the autopsy table, because the condition is not fatal and because few dying of other conditions leave satisfactory roentgenographic records, a less direct method is necessary. An attempt was therefore made to establish its nature by studying its association with other recognizable conditions in the neighborhood.

This apical shadow may be described as a clear line usually seen along the inner surface of the second rib and separated from its shadow by a clear space of perhaps 3 or 4 mm. width. It may also be seen at times beneath the first rib and sometimes it extends downward further into the axilla or becomes continuous with the shadow of the thickened pleura left by a preceding pleural effusion. In width it varies from an exceedingly tenuous line to one of a thickness of 3 or 4 mm. Its density is subject to similar variations; sometimes barely perceptible as a separate shadow, sometimes standing out with striking distinctness. Its differentiation from the linear shadows of the rib margins and the shadows of the overlying soft tissues of the neck requires great care and technically good plates in satisfactory stereoscopic pairs. To see the less obvious examples requires plates of excellent contrast and fine definition.

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[1] Read in brief before the Michigan Trudeau Society, Ann Arbor, Michigan, May 24, 1920.

The study of consecutive sets of plates on the same individual and taken at considerable intervals seems to establish certain definite progressive changes or stages in the development of this shadow with the lapse of time. Not all of these stages can be determined in the same individual, but it is comparatively easy to select out of the accumulated records of the department all the intermediate stages to what appears to be its logical termination.

Beginning with the scarcely perceptible line in the position indicated, one can follow its increased thickness, an indefinite irregularity or mossiness of its visceral surface, followed by the formation of conical or tentlike projections, with the apices directed away from the pleural surface, the formation of long linear shadows from these apices directed toward and reaching the upper cornua of the hilum shadows, the formation of grouped shadows in the periphery of the hilum or in the parenchyma of the lung, and its final obliteration in the increasing confusion of shadows of the chronic tuberculous lung. The order of the later members of the series does not seem to be invariable; in fact, one gets the impression that any of the steps may be omitted or the process become stationary at any stage. The dense conspicuous line, narrow and cleanly penciled, which is the most conspicuous example of the "pleural cap," may very well be the dense residuum of a much wider line resulting from the healing of the process.

One can hardly escape the conclusion that this series represents the progress of a tuberculous infection from the pleura into the parenchyma of the lung. That antecedent stages may occur is indicated by the following case:

A soldier of the selective draft was discharged from Camp Custer with the diagnosis of incipient pulmonary tuberculosis. The Local Board referred him to the Michigan State Antituberculosis Society. The physicians of the Society were unable to discover any physical signs and the roentgenogram also was innocent of any evidence of a tuberculosis of the lungs.

Some time later this man was again referred by the Michigan State Antituberculosis Society, still with the diagnosis of "incipient tuberculosis," and the stereo set demonstrated a subpleural line which a careful scrutiny of the previous plates failed to show. Just one year later he was returned for a third examination, this time from the United States Public Health Service, and this time showing definite involvement of the underlying lung. (No. 21822, J. B., 10/8/19.)

On the other hand, the condition is not infrequently seen incidentally, without clinical evidence of pulmonary tuberculosis and without evidence of change over considerable periods of time. We believe that under these circumstances we are justified in considering such shadows as representing an organized and healed lesion, an evidence of a preceding infection but without significance as to the present health of the individual.

Such cases presumably are the equivalent of the relatively numerous autopsy findings showing thickening of the apical pleurae, parietal or visceral, with or without adhesions. These are generally held by the pathologist to represent a healed tuberculosis, even though the demonstration of the characteristic microscopic lesion is impossible. The general acceptance of this interpretation is to a large degree responsible for the dictum, *Jeder Mann hat am Ende ein bischen Tuberkulose.*

Statistics comparing the frequency of the radiographic and the pathological lesions should show the former relatively less frequent, since the pleural thickenings are manifest on the plate only when seen tangentially and favorably placed in the immediate and contrasting relationship with a landmark like the rib. Obviously one could not expect to find it over the mesial surface of the upper lobe where it would lie against the soft tissues of the upper mediastinum which have approximately the same density to the ray. Nor can it be seen on the anterior and posterior surfaces of the apex, where the increment of its density is sufficient to impress an appreciable shadow on the relatively greater shadow of the chest wall and its contents. The number of cases in which the thickening of the pleura occupies a favorable site must therefore fall far short of the total number.

In this study we hope to present some data tending to prove the tuberculous nature of this cap and suggesting that it results from a downward extension of the infection from the cervical lymphatics after its entry through the lymphoid tissues of Waldeyer's ring.

The faucial tonsil was suggested as the portal of entry for the tubercle bacillus as early as 1897 (1). However, this path of infection has not been generally accepted as an important one and the ingestion hypothesis has been brought forward to explain the transmission of tuberculosis as against the inhalation theory.

Most of the earlier clinicians (2), from clinical evidence alone, believed that the tubercle bacillus passed from the cervical lymph glands to the bronchial glands, and from there in some manner (as a rule by the blood stream) to the lungs. Another group (3), however, believed that the tubercle bacillus reached the supraclavicular glands from the pharynx and passed from there directly to the apices of the lungs. Grober (4) especially made an elaborate study on dogs and guinea pigs to show the possibility of direct infection through the tonsil. He injected the pharyngeal wall of these animals with india ink and killed them at varying intervals after the injection. He found that the particles were carried down the cervical lymphatic chain directly to the apical pleura and through the apical pleura to the lung parenchyma. Beitzke and Most (5) criticized this work on anatomic grounds and further denied any connection between the cervical and bronchial glands, thereby opposing the ideas of both groups of clinicians before cited.

Trautmann (6) accepts the criticisms of Beitzke and Most, but he admits the possibility of infection of the cervical glands by the tonsillar route.

G. B. Wood (7), however, has shown that there is a continuous lymphatic path from the tissues of the pharynx to the apex of the lungs, and Miller (8) has shown that the lymphatic drainage of the pleurae is towards the hilum.

In attacking this problem we have collected evidence which points to an intimate relationship between the occurrence of tubercles in the faucial tonsil and the so called pleural cap.

All the tonsils removed at the University Hospital, in the service of Dr. R. B. Canfield, are examined by the Department of Pathology in the service of Dr. A. S. Warthin. One section only of each tonsil is examined, but this is so cut that it includes almost all the crypts. Some cases of tuberculosis of the tonsil are undoubtedly missed in this routine examination, but the number is probably not great. Serial sections would probably be the most certain method but this is too laborious in a large series. Injection of the macerated tonsil into guinea pigs is even more arduous and therefore not a feasible method for application on a large scale, although by this method A. P. Mitchell (9) was able to demonstrate tubercle bacilli in 37.5 per cent of his cases of tuberculosis of the cervical glands.

In the period covered by this study we were able to examine by the X-ray the chests of 16 individuals who had proved tuberculous lesions in their tonsils. This small number out of the many which form the basis of a report which Dr. Carl V. Weller has in preparation is explained by the difficulty of reaching these patients after the delay necessary for the completion of the pathological examination. Of these 16 cases all but one showed a pleural cap. This is rendered more significant when we consider 27 chest examinations on patients whose extirpated tonsils were found to be free from tuberculosis, and of these only 3 disclosed a pleural cap and 24 did not. Of the 3 of this latter group who did show the cap, none showed more than a relatively fine line without recognizable evidence of tuberculosis in the underlying lung.

That a similar relationship exists between the pleural cap and cervical gland tuberculosis is shown by the series collected by Dr. Robert Baker from the service of the Department of Surgery. Of the 28 cases clinically diagnosed tuberculous, 16 showed a pleural cap, 4 more showed a degree of involvement of the apices in a pulmonary tuberculosis which would mask this shadow of the pleural cap, and 8 escaped without evidence of the invasion of the chest. It should be noted that the clinical diagnosis was not in every case established beyond doubt and the possibility of the nontuberculous nature of these 8 cases cannot be excluded.

TABLE 1

The relative frequency of pleural caps in the three series of cases studied. It is to be noted that in the case of cervical adenitis 71 per cent of the total showed signs in the lungs; in the cases of tuberculosis of the tonsil those showing frank tuberculosis also showed a pleural cap

SERIES	PLEURAL CAPS	NEGATIVE FOR TUBERCULOSIS	FRANK TUBERCULOSIS
	per cent	*per cent*	*per cent*
Tonsillar tuberculosis	93	7	25
Negative tonsils	11	89	0
Tuberculous adenitis, cervical	59	29	12

We are unable to supply data as to the occurrence of tonsillar tuberculosis in this particular group of cases but reliable evidence (10) is available to show that the cervical glands become infected through the lymphatics of the neck and the lymphoid tissue of the pharynx in almost every case.

To ascertain the frequency of the pleural cap in other conditions, the chest radiograms made in the laboratory over a typical three months' period were reviewed. This phase of the question will be discussed in a later paper when a more careful study has been completed. A hasty survey of the notes but without a review of the original plates gives the following data.

Out of the 318 records examined, an apical pleuritis was noted in 43, and a frank and extensive tuberculosis often masking the region of the apical shadow was noted in 78. Thirty showed an apical pleuritis as the sole finding suggesting tuberculosis. If one may assume that this pleuritis is tuberculous in nature, one reaches the conclusion that of the 318 cases examined during this three-month period, 103 showed evidence of tuberculosis and of these at least 40 per cent showed a pleural involvement. It is to be emphasized that this percentage is minimal for the reasons already mentioned above.

Various statistics are available as to the occurrence of tonsillar tuberculosis. This lesion was first described by Orth (11) in 1879. In 1905, G. B. Wood (12) collected published statistics of 1871 tonsillectomies for all causes and found that 5.2 per cent were tuberculous. In this study it was found that 69 per cent of the cases having pulmonary tuberculosis also had tuberculosis of the tonsil. Smearing a culture of tubercle bacilli over the tonsils of pigs caused a cervical adenitis and tuberculosis and although he was able to recover the organisms from the digestive tract, the mesenteric glands were never infected in these experiments. He concluded that the pulmonary lesions arose by haematogenous metastasis from the cervical glands. From our point of view it seems much more likely that the spread was similar to, and followed a path like that taken by, the india ink particles in Grober's experiments.

TABLE 2

The distribution of lesions in all the chest radiograms made in the laboratory over a three months period, taken from the records without reviewing the plates

	CASES
Apical pleuritis alone	39
Apical pleuritis plus frank tuberculosis	13
Tuberculosis (no pleural cap noted)	60
Negative for tuberculosis	215
Total	318

B. C. Williams (13) made a careful histological study of the faucial tonsils of 29 cases of tuberculous cervical adenitis and was able to demonstrate tuberculous lesions in 86 per cent. Unfortunately he did not study the lungs in this connection.

The foregoing figures warrant the conclusion that the lymphoid path of infection is possible, and that such descending infection is the rule in cases of cervical adenitis following a primary infection of the faucial tonsil. The question naturally arises as to the importance of this path in the transmission of pulmonary tuberculosis. The data given in table 2 indicate that the relationship between the apical cap and pulmonary tuberculosis is an exceedingly close one, and this relationship is difficult to explain on any other hypothesis than that of a direct lymphogenous metastasis through the cervical chain.

The inhalation theory seems entirely inadequate since the organism can only reach the pleurae from its primary lodgment in the lower bronchi by metastasis against the prevailing lymph stream, and one fails to find a determining factor directing the stream towards the apex rather than to some other portion of the pleural cavity. The haematogenous route, after ingestion of the organism into the gastrointestinal tract, similarly lacks evidence of a directive force causing the selection of the apical pleura as the seat of final lodgment, while the lymphogenous route after ingestion requires an itinerary so devious and indirect as compared with the route by the cervical chain as to arouse our skepticism.

Lexer (14) has shown that the microörganisms can enter the body through the tonsil and leave no trace in that organ. The adherents of the ingestion theory of tuberculous infection have postulated such behavior on the part of the tubercle bacillus with respect to the lymphoid tissues of the intestinal canal. As a matter of fact, the tonsils form only a fraction of the total lymphoid tissue in the pharynx and we have no reason to suppose that the behavior of the tonsil or of the remainder of the lymphoid tissue of the neck is in any way different from that of the gut. The occurrence of apical caps in 11 per cent of the cases in which no tuberculosis was found (table 1) therefore need cause no great surprise. By an extension of this line of reasoning it is entirely conceivable that many cases of pulmonary tuberculosis have been infected by this route without leaving any trace along the route except at the apical pleura.

Our general impression is that the pleura offers a considerable barrier to the further progress of the infection and that the disease is frequently arrested at this point. There are a sufficient number of serial studies now at hand in the archives of the Department of Roentgenology to demonstrate the quiescence of the denser type of "pleural cap" over a considerable period of time. We are not prepared to formulate our ideas on this subject further than to express the opinion that the denser and the more sharply defined and delimited the shadow, the more nearly harmless it is. On the other hand, we view with suspicion those "caps" which are lacking in density and show irregularities on the visceral surfaces as indicating a process not yet fully cicatrized and progressing along the connective tissue elements of the lung parenchyma.

We believe the figures here presented show a close relationship between the lesion in question and pulmonary tuberculosis and that a more careful review of the original plates will probably show a still more convincing relationship. For it is probable that many pleural caps have failed to be recorded in the routine survey of the laboratory or have been overlooked in the confusion of shadows commonly seen in the extreme apex in cases of frank tuberculosis. We are planning to make a complete survey of this sort in the immediate future and to continue this study both experimentally and clinically.

SUMMARY

1. A shadow that we believe represents a thickening of the pleura over the apex of the lung has been described and its relationship to tonsillar and cervical gland tuberculosis has been studied.
2. Such an apical pleuritis is seen in at least 10 per cent of all X-ray examinations of the chest coming to the University Hospital laboratory.
3. Such apical pleuritis occurs most frequently in cases showing tuberculous deposits in the faucial tonsils (93 per cent).
4. With the cervical gland tuberculosis this lesion is recognizable in 59 per cent of all cases and probably occurs in a larger number, being obscured by the shadows of pulmonary tuberculosis, 71 per cent in this group showing either this lesion or frank tuberculosis of the lung or both.
5. Cases without tuberculosis of the tonsil show an apical pleuritis in only 11 per cent of the cases.
6. It is suggested that a common route of infection may lie through the tonsil and cervical lymphatics to the apical pleura and thence into the lung. If this hypothesis is accepted it offers a singularly satisfactory explanation for the frequency of apical lesions, the predominance of right-sided lesions, of the pathogenesis of tuberculous pleurisy with effusion and other obscure features of this infection.

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A CONSOLIDATED MEDICAL REPORT COVERING DISCHARGES FROM THIRTEEN MINNESOTA COUNTY SANATORIA

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Those interested in the institutional treatment of the tuberculous will appreciate the great importance of complete and accurate records. Not only are such records important to show the results obtained in each institution but every sanatorium operating as part of a state's system, or better, all sanatoria should maintain the same system of medical records to permit not only of comparison but of a consolidation of reports.

A detailed account of patients' records in use in the 14 county sanatoria in Minnesota[1] was published in *The Modern Hospital, vol. 12, no. 1, January, 1918.* Figure 13 in the *Modern Hospital* report shows the form upon which institutions report on all discharged cases to the Advisory Commission. It is from these individual reports that the Advisory Commission compiles the annual medical report of each institution and from these the consolidated report dealt with in this paper. The period covered is twelve months, ending September, 1920.

From a study of table 1 it will be noticed that 664 patients remaining over thirty days for treatment were discharged or died during this twelve month period. The average residence was a little over thirty-one weeks. This is, we believe, a record for institutions caring for all stages of tuberculosis, giving preference to the Far Advanced, and tends to show that conditions at these institutions were such as to produce contentment and willingness for prolonged treatment.

We may first take the 99 Incipient cases mentioned in table 1. First, it will be noted that all but 7 are classified according to the Rathbun classification of the National Tuberculosis Association method, which is understood by all. We have no explanation to offer in failing to so classify 7. Eighty-nine of these have negative sputum, out of which number 3 were progressive cases on discharge, although 6 cases were admitted as having "C" symptoms. Ten Incipient cases have positive sputum and of these 3 were progressive cases on discharge, with "C" symptoms on admission. It will be noted that no Incipient case with positive sputum was discharged with a better result than Quiescent.

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[1] There are 14 county sanatoria in Minnesota under the supervision of the Advisory Commission. Reports from one were received too late to be included in this paper.

TABLE 1

CLASSIFIED ACCORDING TO						ALL PATIENTS WHO STAYED OVER 30 DAYS									
Lesion		Symptoms			Turban	Sputum	Cases	Apparent cure	Arrested	Apparently arrested	Quiescent	Improvement	Progressive	Died	Average residence
		A	B	C											
															weeks
Incipient	7	58	18	6	I	0	89		12	39	11	24	3		26+
		6	1	3	I	+	10				2	5	3		32+
						*									
					‡										
Moderately advanced	3	11	3	3	I	0	20		2	4	2	10	2		33
		2	2	1	I	+	5					2	1	2	30+
	2	41	42	7	II	0	92		8	22	22	31	7	2	38
	5	30	40	34	II	+	109				9	43	33	24	32+
	1		1	1	III	0	3					3			24
	1	2	12	5	III	+	20					6	5	9	22+
						*									
					‡										
Far advanced					I	0									
				2	I	+	2							2	10
	1		3	2	II	0	6				1	3	2		20+
	2	2	16	8	II	+	28					9	8	11	28+
	1	10	11	29	III	0	51		2	2	3	14	5	25	29
	10	19	50	149	III	+	228				4	43	43	138	30
			1			*	1					1			56+
					‡										
Total.......	33	181	200	250			664		24	67	54	194	112	213	31+

* = No sputum report available. ‡ = No Turban classification. Cases not reported, owing to lack of information.

Total average for all cases (967) for year 28 weeks. Including 132 nonpulmonary tuberculosis cases or nontuberculous cases not tabulated.

In fact, if the table is followed through the same applies to all cases with positive sputum. We have the Annual Medical Report for the Minnesota State Sanatorium for the year ending December 31, 1917. This report also shows that no positive sputum case was discharged better than Quiescent.

The value of Rathbun's modification of the old classification of pulmonary tuberculosis is clearly shown in table 1, under Moderately Advanced cases. Taking those of the "C" class and studying their results as shown by Progressive and Died, we find the classification is fairly well borne out by the final results.

The large number classified as Far Advanced, 316, indicates the great value these sanatoria are to the local communities in which they are located. Nearly one-half of the total discharged were Far Advanced. Of these 316 Far Advanced cases, 176 died and 58 others failed of being benefited by treatment, leaving 82 Far Advanced cases to be helped. Some of these "improved" cases are so classified because of the form of treatment received, namely, artificial pneumothorax. We do not classify cases so treated as better than Improved on discharge. Of the grand total 664, in table 1, there were 325 Progressive or Died on discharge or 48 per cent. However, 234 of these were admitted as Far Advanced and 190 of the 234 were in the "C" class.

TABLE 2

Time of residence for all cases

CLASS	CASES	15 DAYS OR LESS	15 to 30 DAYS	1 MONTH TO 3 MONTHS	3 MONTHS TO 6 MONTHS	6 MONTHS TO 9 MONTHS	9 MONTHS TO 12 MONTHS	12 MONTHS AND MORE	AVERAGE RESIDENCE
									days
Incipient	125	17	9	27	29	19	10	14	134
Moderately advanced	287	23	15	68	70	32	23	56	216
Far advanced	423	61	46	105	93	41	23	54	180
Total	835	101	70	200	192	92	56	124	188

1 incipient case died, average residence 3+ weeks.
39 moderately advanced cases died, average residence 37+ weeks.
242 far advanced cases died, average residence 41+ weeks.

Passing to table 2, in column headed "15 days or less" and "15 to 30 days," there are listed those not reported in table 1, because of their short length of residence. There were 171 who left in less than thirty days. As there were 282 total deaths, of which 213 occurred after thirty days' residence, we have 69 deaths occurring before thirty days have elapsed. If we eliminate these 69 deaths from consideration, we have 102 living cases leaving the institution within thirty days of admission, or 12.2 per cent of the total number discharged, which is 835. This small percentage we believe is a record. Retaining the number of deaths, which is 69, and using the total 171, with residence less than thirty days, we get 20 per cent of all patients remaining less than thirty days. We know of only one report from a state group of county sanatoria reporting on this feature; and the percentage of discharges in thirty days or less was 35.47.[2] The total number of cases referred to was 409, of which number 129 represent deaths, giving 24 per cent of living cases leaving in less than thirty days, compared with 12.2 per cent from the Minnesota sanatoria. However, the records should be much better. Twenty-six of our Incipient cases failed to remain thirty days or longer. Why? Only one death occurred in this group, so there remains 25 Incipient cases to explain the failure to hold. Every sanatorium man encounters new patients who refuse to remain, some because of homesickness, disappointing surroundings or the presence of others with advanced disease, and some simply because they are neurotic and are difficult to satisfy or to impress with their responsibilities. However, a greater effort should reduce the number of such failures.

TABLE 3

Condition of sputum (positive or negative) for all discharged

CLASS	CASES		APPARENTLY CURED	ARRESTED	APPARENTLY ARRESTED	QUIESCENT	IMPROVED	PROGRESSIVE
Incipient	13	Pos.				2	5	6
	108	Neg.		13	41	12	28	14
Moderately advanced	122	Pos.				9	56	57
	123	Neg.		10	26	24	44	19
Far advanced	135	Pos.				5	55	75
	43	Neg.		3	2	3	23	12
Total	270	Pos.				16	116	138
	274	Neg.		26	69	39	95	45

3 incipient cases not included in above report due to lack of information.
3 moderately advanced cases not included in above report due to lack of information.
3 far advanced cases not included in above report due to lack of information.

Table 3 shows the condition of the sputum on discharge of all living cases with the results of treatment. It will be seen that of a total 544, 270 had positive sputum and 274 negative sputum on discharge.

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[2] Amy L. Mercer, Bureau of Tuberculosis Hospital Admissions and Discharges, *Transactions of the Thirteenth Annual Meeting of the National Association for the Study and Prevention of Tuberculosis.*

Attention is called to the 45 negative sputum cases discharged as Progressive as against 138 positive cases so classified. Note also the failure to discharge any positive sputum case better than Quiescent, while 69 negative sputum cases were Apparently Arrested and 26 Arrested.

TABLE 4

Results of sputum examinations

CLASS	EXTENT OF PHYSICAL SIGNS ACCORDING TO TURBAN	CASES	TREATMENT	255 A † R † D †	25 A † R † D O	2 A † R O D †	19 A † R O D O	7 A O R † D †	4 A O R O D †	13 A O R † D O	190 A O R O D O	26 P † A O R O D O
Incipient	I	120	Without tuberculin	9	3	1	5	3		2	83	2
	I		Tuberculin over 90 days		1		1				2	
	I		Tuberculin 90 days or less							1	5	2
Moderately advanced	I	243	Without tuberculin	4	3		1			2	17	
	I		Tuberculin over 90 days								1	
	I		Tuberculin 90 days or less									
	II		Without tuberculin	95	9		4	1		3	54	13
	II		Tuberculin over 90 days	2	3						3	
	II		Tuberculin 90 days or less	4		1		1				1
	III		Without tuberculin	12	1		1			2	3	
	III		Tuberculin over 90 days	1								
	III		Tuberculin 90 days or less								1	
	‡		Without tuberculin									
	‡		Tuberculin over 90 days									
	‡		Tuberculin 90 days or less									
Far advanced	I	178	Without tuberculin									
	I		Tuberculin over 90 days									
	I		Tuberculin 90 days or less									
	II		Without tuberculin	17							3	1
	II		Tuberculin over 90 days									
	II		Tuberculin 90 days or less						1			
	III		Without tuberculin	109	4		7	2	3	3	16	7
	III		Tuberculin over 90 days	2								
	III		Tuberculin 90 days or less		1						1	
	‡		Without tuberculin								1	
	‡		Tuberculin over 90 days									
	‡		Tuberculin 90 days or less									

1 incipient case, 2 moderately advanced cases not reported due to lack of information.

O = Tubercle bacilli absent. † = Present. A = Admission. R = During residence. D = On discharge. P = Previous to admission. ‡ = No Turban classification.

When tubercle bacilli were present on admission, no note is made with regard to previous examinations. When tubercle bacilli were present previous to admission, and also at any time during residence, they are marked as present on admission.

The total number discharged with positive sputum brings up the question of home infection again, and the proper step to take which would be a fair one to the individual as well as to the public. Is it the industrial colony medically supervised? Not considering the 138 progressive cases with positive sputum, we would have 132 positive sputum cases, the majority of which would be suitable for colonization. This number available each year from our group of sanatoria, all with positive sputum, would at least seem to prove the need of some such arrangement for their care and for the public good. The 138 positive sputum cases discharged as progressive should of course not have been discharged at all, but should have remained in the sanatoria, and represents as great if not greater failure on our part than the 102 cases who failed to remain thirty days or longer.

As this paper deals with the value of accurate and complete sanatorium records we will include here the results of the financial reports received by the Advisory Commission from the several institutions each month, as the figures may be of interest at least to sanatorium administrators.

The average cost per patient for maintenance only, for all the sanatoria in the year 1919, was $2.62. After deducting receipts from all sources the net cost to the counties maintaining the sanatoria was $1.67 per day per patient. These figures do not include permanent improvements, enlargements, etc., but do include all maintenance expenses. The figures for the first six months of 1920 were $2.89 as the cost per day per patient and $1.80 as the net cost after subtracting receipts. The average cost per meal per individual for raw food was only 19.8 cents for 1919. The average cost served per meal was 22.3 cents for the same period. This latter figure includes the cost of buying, cooking, serving and maintaining of culinary department. For the first six months of 1920, we have 20.9 cents as the average cost per meal for raw food and 23.7 cents served. It has been our experience that the difference in cost between the raw food and the served meal was two or three cents per meal. This would appear correct from the reports from our sanatoria.

CONCLUSIONS

1. Complete and accurate medical reports from each sanatorium are of great value, while similar records from a group which can be consolidated in one comprehensive report are of still greater value.

2. The average length of residence (31+ weeks) is exceptionally good but should be increased.

3. The best results, Arrested and Apparently Arrested, are with the Incipient and Moderately Advanced cases with negative sputum.

4. The county sanatorium is proving its value to the community: 52 per cent of all cases admitted, remaining over 30 days, were benefited by treatment.

5. From a total of 402 positive sputum cases, remaining thirty days or longer, 186 died and in 93 the disease progressed, leaving 123 as being benefited. It should be remembered that of these 402 positive sputum cases, 258 were classified as Far Advanced on admission, 159 of these in the "C" class, 134 more were Moderately Advanced and 40 of these were in the "C" class. Thus there were a total of 199 in the "C" class (Moderately Advanced or Far Advanced) to account for the 186 Moderately Advanced and Far Advanced who died. This only illustrates the class of patients being admitted to these sanatoria which is as the state law provided, namely, preference being given to advanced cases.

6. The Rathbun modification of the National Association classification has proved to be a great improvement, as shown by the end results.

7. Twenty per cent of Incipient cases failed to remain thirty days or longer (no deaths included): 12+ per cent of Moderately Advanced cases failed to remain 30 days or longer (no deaths included): 9 per cent of the Far Advanced cases failed to remain thirty days or longer (no deaths included): 12.2 per cent of all cases remained less than thirty days (no deaths included).

8. On discharge 270 cases had positive sputum while 274 cases had negative sputum. On admission or during residence, 83 had positive sputum; but negative sputum on discharge. Eleven had negative sputum on admission but positive sputum on discharge.

9. A solution of the positive sputum case on discharge must be found. At present the writer favors a state industrial colony for a certain percentage of these.

10. We are not getting Incipient cases into sanatoria in large numbers.

11. The number of cases remaining less than thirty days is too many and must represent wasted money and effort on the part of the institution.

12. Although 83 patients were admitted with positive sputum or had it during their residence and were discharged with negative sputum, none of these were discharged with a better result than Quiescent (see tables 1 and 4).

13. The number of active cases with positive sputum restored to health, compared to those so afflicted in and out of our institutions, is much too small to have any considerable influence on the decline of the death rate from tuberculosis.

14. The number of positive sputum cases which do not have the opportunity either before or after sanatorium treatment for infecting others in the family is exceedingly small. Thirteen cases had positive sputum during treatment but negative on admission and discharge, compared to 528 with positive sputum either on admission or on discharge.

15. From the above it is plain that the ideal, for sanatorium care to prevent the spread of infection, is not attained and will not be until (1) the case is admitted before the sputum becomes positive and (2) proper solution is found for the control or supervision of the positive sputum case after discharge.

SUNLIGHT AND ARTIFICIAL LIGHT THERAPY IN TUBERCULOSIS

A CRITICAL REVIEW

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The application of light, both natural and artificial, in tuberculous affections has gradually come to assume enough importance, particularly among foreign workers, to call for special consideration. The writer has therefore attempted a résumé of the subject, in an endeavor to learn what may be considered its present position in treatment. There has and always will be, in medicine, two extremes: the one refusing ever to consider a new mode of treatment which had not proved useful in earlier years; and the other grasping only too soon whatever new treatment may be offered. To strike the happy medium is, of course, our endeavor. Light therapeusis is not, however, as recent a procedure as one is at first prone to believe.

HISTORICAL

One already finds mention of the value of the sunlight in the writings of Herodotus and Hippocrates. The ancient Egyptians worshipped their sun god. The Greeks and Romans built solaria in their homes and on their terraces. However, very little attention was otherwise given to sun treatment until the French revived it shortly before 1800. We then meet with the publications of Bertrand and Leconte, and following these, of von Löbel, Cauvins and Dobereiner. In 1801, Ritter reported the action of ultraviolet rays upon silver chloride. In 1818, Grotthus formulated his law, "Only the rays absorbed are effective in producing chemical change." About 1840, Ollier and Poncet of Lyons published their observations on the treatment of tuberculous arthritis with sunlight. Bonnet, about the same time, advised sunlight for arthritic cases as the treatment of choice, and emphasized the general raying of the body. Rickli, in 1855, in Switzerland, also published his article on the "Atmospheric Cure." It was not until 1899 that the actual importance of this treatment was realized, when Finsen published his work upon the violet and ultraviolet rays in the therapy of lupus as well as the treatment of smallpox with the red light. Following him, in 1902, Bernhard of St. Moritz, impressed by the custom of the Swiss butchers, who cured their meat in the sun, treated in this way an Italian with a suppurating wound of the abdomen. The healing of this case was so remarkable that all other wounds were similarly treated. Bernhard soon afterwards issued his publications on his surgical cases treated by exposure to sunlight. Ignorant of Bernhard's work, Rollier in Leysin, in 1903, began treating his tuberculous cases in the same way. For four years previously he had worked as assistant to Kocher. In 1904 Malgat at Nice first tried the treatment of pulmonary tuberculosis with sunlight. Morin a little later applied the same treatment for pulmonary tuberculosis of children. In 1911 Bardenheuer in Cologne and Escherich in Vienna first gave their reports on the use of sunlight in the lowlands; and von Schrötter followed them with the publication of his experiments.

The first real stimulus to artificial light therapy was Finsen's work. He used the carbon arc light for the treatment of lupus, in which he emphasized the importance of the violet and ultraviolet end of the spectrum. In 1892 Arons first learned that a container with mercury vapor, if electrified, emitted a bluish light which had no red or orange rays. Following this Cooper Hewitt patented his glass lamp based on Arons's discovery. Then Heraeus succeeded in melting quartz crystals, so that quartz containers were soon made by Küch and others. In 1904, Kromayer was among the first to therapeutically use the quartz light, attempting, after Finsen's work, to apply pressure lenses and use water-cooling attachments; so that during subsequent years other lamps were manufactured in accordance with his suggestions, culminating in the present Kromayer lamp.

Nagelschmidt, of the Finsen clinic, first worked along the lines from which the final mercury quartz lamp was constructed. Bach later tried to modify it, attempting to use the ozone generated by the lamp but this proved unsuccessful.

THE COMPONENTS OF SUNLIGHT AND THEIR PROPERTIES

When passed through a prism sunlight splits up into its individual rays. The visible spectrum is made up of the red, orange, yellow, green, blue, indigo and violet colors; the invisible consists of the infrared and ultraviolet rays.

Figure 1 is a graphic representation of the rays with their respective positions in the spectrum. The rays are considered in terms of their wave length and number of oscillations per minute. The wave lengths are generally designated in terms of *micra, millimicra* or *Ängstrom units.*

Schunck divides the regions of the spectrum into the following:

	Ängstrom units ($\frac{1}{10}$ $\mu\mu$)
Visible region	7594–3934
Ultraviolet region	3934–1850
Schumann region	1850–1230
Lyman region	1230–600
Unexplored region	600–8
X-rays and gamma region	8–0.07

Richardson and Bazzoni are supposed to have recently extended the known region from 600 to 420 A. U.

The *infrared rays* lie between 130μ and 800$\mu\mu$. Their chief action is to produce warmth. They may possibly also produce chemical changes and be bactericidal; but their immediate effect is a widening of the blood vessels, with an increased amount of blood brought to the skin, and increased sweating. Redness occurs, and blisters can be produced. There is no latent period. The reaction occurs immediately after the rays are absorbed; and the biologic changes immediately disappear after a discontinuance of the exposure. They are selectively absorbed by humidity, as is shown by the water-absorption bands. It is hoped that more will be learned about these rays, for they may possess very important functions that are at present not understood. The gap between 130μ and the Hertzian or electric waves has not yet been worked out.

Light rays, extending from 800$\mu\mu$ to about 400$\mu\mu$, make up the visible spectrum. When they are exposed to the retina, there is a definite latent period before the light reaction occurs. This latent period varies with the intensity of the light. The rays show themselves only through their physiologic action and leave no lasting traces on the rayed cells. They have good penetrating power, which is greatest at the red end of the spectrum. This end has the longest wave lengths and the smallest number of oscillations. It is the heat-producing end, while the violet is the chemical end. The reds produce a hyperemia immediately upon raying, and this disappears soon after exposure.

Beyond the violets, extending from about 380$\mu\mu$ to about 60$\mu\mu$, we find the ultraviolets. In sunlight these extend to 291$\mu\mu$. With very short wave lengths they easily produce chemical changes; but a definite

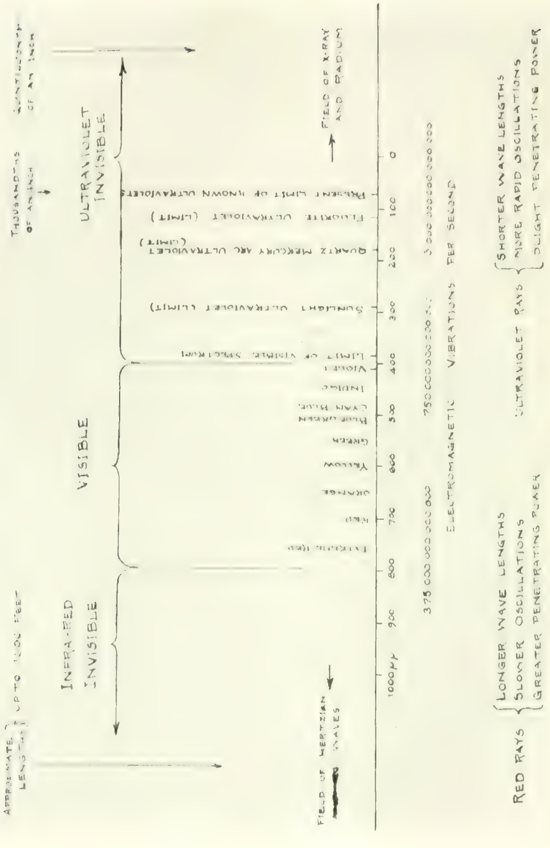


Fig. 1. Graphic Representation of the Visible and Invisible Rays, with Their Respective Properties

latent period exists before the erythema set up by them appears. Bacteria are easily affected by them, an action well detected with the ultramicroscope. If one places organisms before the Kromayer lamp, movements of bacteria are seen to stop and death may result. The Brownian movement of colloidal particles in albumin molecules is quickly inhibited, evidently by a process of coagulation; and the cells are killed. These ultraviolets are the pigmenting rays, the best ones occurring around $300\mu\mu$. Those below $290\mu\mu$ are much more irritating; and, as a result, have a tendency to set up a severe erythema unless the dose is carefully graded.

TABLE 1

Regional division of ultraviolet rays (*Shepard*)

REGION OF WAVE LENGTHS IN $\mu\mu$	DENOMINATION (OR ABBREVIATED DENOMINATION)	REMARKS ON CHARACTERISTICS AND SOURCES
500–440	Blue	Visible
400–380	Violet	Visible
380–340	Glass ultraviolet (glass-violet)	Transmitted by ordinary glass in moderately thick layers; profusely emitted by electric arc with carbon poles
340–300	Jena-glass-ultraviolet (Jena-glass-violet)	Transmitted by Jena ultraviolet crown glass; profusely emitted by uviol mercury lamp
300–220	Quartz glass ultraviolet glass (quartz glass violet)	Transmitted by fused quartz (and calcspar) in not too thick layers; the last portion of the emission of quartz mercury and quartz amalgam lamps
220–180	Quartz crystal ultra violet (crystal violet)	Transmitted by moderately thick layers of crystalline quartz (also by gypsum and rock salt); can be decomposed in the quartz-spectograph
180–120	Fluorspar ultraviolet (Schumann violet)	Still transmitted by good fluorspar, but completely absorbed by short air spaces; decomposed in vacuum spectrum apparatus with fluorspar media
120–90	Reflex ultraviolet (reflex violet)	Strongly metallically reflected from all the above mentioned solid media, according to theory of dispersion only to be investigated in their absence; dispersable with reflection grating (Lyman)
Shorter waves	Transreflex violet	Unknown

All the rays of the spectrum have some slight warmth and chemical properties. Beyond the ultraviolets of $180\mu\mu$ are seen the fluorite ultraviolets or Schumann's region (see table 1). Quartz or rock crystal glass is permeable for the ultraviolets down to $180\mu\mu$, while fluorite is permeable for those of Schumann's region. The shortest known ultraviolets are those of Lyman, only recently explored. Beyond the ultraviolets one gets into the field of the X-ray, and beyond this into the field of radium light vibrations. At the long end of the spectrum are the longest rays, which give us wireless waves, first described by Hertz in 1886. These are considered to be electrical waves because an apparatus such as the Leyden jar can produce them. They are really waves of the ether. The existence of other waves, known as the N waves (described by Blondlot of Nancy), formerly believed to exist either near the wireless waves or at the opposite end of the spectrum near the X-rays, has been disproved. The chemical effect of the ultraviolets upon bacteria is similar to their action upon proteins: a soluble protein easily becomes an insoluble one. This action will be considered under experimental work. There is a sharp difference between the effects of the ultraviolets of $300\mu\mu$ and those of $290\mu\mu$ upon proteins, as shown by Henri, and upon bacteria, as shown by Russ. The former may barely produce changes while those around the latter, (and below), can show great chemical and destructive power.

The ultraviolets, in passing through air, are easily absorbed, reflected and bent by impurities such as smoke, gases, dust, humidity, etc. Even mere passage through atmosphere itself causes a splitting off by a scattering. In contrast to the reds, the ultraviolets are quite easily reflected and absorbed. The law of reflection no longer applies when the particles in the air are smaller than the length of the rays.

There is probably a specifically greater variability in the intensity of the ultraviolet region as compared with the other parts of the spectrum. The disturbing factor is the variation of the transparency of the atmosphere for these rays. The transparency to the ultraviolets appears to depend chiefly on the presence of condensed water particles. Condensation produced by the cooling due to expansion occurs much more readily in nucleated air than in air free from nuclei. Aitken considers that dust alone is sufficient to account for atmospheric condensation. Arrhenius and others say that nucleation by ions plays an important rôle: the ionization may be secured chiefly by the discharge of negative electricity by ultraviolet light at the earth's surface or by direct ionization of moist air by ultraviolet light. The action brings about, as it were, an autocatalysis of the absorption of ultraviolet light by the atmosphere. The ozone content of the atmosphere is another variable factor, since ultraviolet light affects it. (Bayliss.)

Outside of our atmosphere the transparency to ultraviolet depends chiefly on the ozone content. Water vapors and air have about the same absorption power, the limit being $170\mu\mu$.

The most suitable substances for reflecting the ultraviolets are platinum, nickel, silicon and an alloy of magnesium and aluminum. Snow, ice and water also enhance the powers of these rays by reflection, so that the greatest intensity exists at the seashore and high altitudes. After snowfall, light intensity is greatest. The deserts and prairies may also be rich in ultraviolets.

Warmth and light intensity decrease progressively from the equator to the poles. The greatest possible yearly sunshine has its nearest approach at Kimberley in South Africa, which possesses 3200 hours out of a possible 4380 hours.

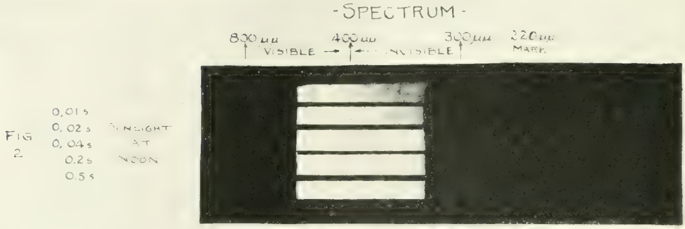
PENETRATION

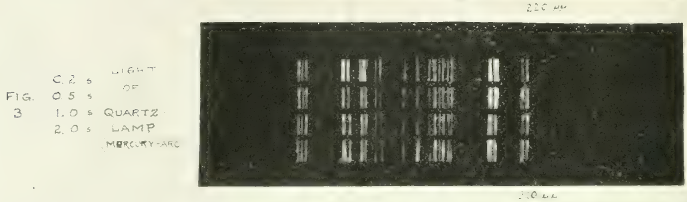
Many divergent opinions exist in regard to the exact penetrating power of the various light rays. Hasselbach offers the following scale for the ultraviolets:

	VIOLET	ULTRAVIOLET						
Wave Length, $\mu\mu$	436	405	366	354	313	302	297	289
Thickness: Skin, 0.1 mm	59.0%	55.0%	49.0%	42.0%	30.0%	8.0%	2.0%	0.01%
Thickness: Skin, 1.0 mm	0.5%	0.3%	0.08%	0.02%	—	—	—	—

Here the penetration from 313$\mu\mu$ down is seen to decrease rapidly. There is 70 per cent loss at 313$\mu\mu$, 92 per cent loss at 302$\mu\mu$, and practically 100 per cent loss at 297$\mu\mu$.

Before taking up other opinions on penetration, it is necessary to consider figures 2, 3 and 4 by Schanz showing the spectra of sunlight, the quartz mercury arc and the open carbon arc respectively. These were taken with a quartz spectrograph, the sunlight pictured at noon in Dresden. The visible spectrum extends roughly to 400$\mu\mu$, the invisible or ultraviolets of sunlight reach to about 290$\mu\mu$, and the ultraviolets of the mercury and carbon arc to 220$\mu\mu$. Because of the dense atmosphere at the time, many ultraviolets of sunlight were unfortunately lost, while the reds and ultrareds were not picked up by this spectroscope. Figure 3 shows the spectrum of the quartz mercury light (according to Schanz) as a line type, discontinuous, and in contrast to the continuous one of sunlight (see also figure 5). Figure 4 shows that the carbon arc, which will be considered later, contains all the ultraviolets of the mercury light and has a continuous spectrum like that of sunlight. It contains also the red rays of sunlight. (The reds are not shown here because the photographic plate was not sensitive enough on these short exposures.)





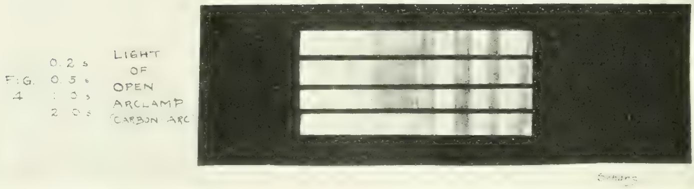


Fig. 2. Solar Spectrum Photographed with a Quartz Spectrograph in Dresden at Noon

The exposures were not long enough to detect the red rays; the ultraviolets in sunlight, which ordinarily extend to about 290μμ, were also not completely photographed with these exposures.

Fig. 3. Spectrum of the Quartz Mercury Arc

It is a band type, discontinuous, extending to 220μμ. The red end of the solar spectrum is not present in the quartz mercury light. Additional short ultraviolets are found.

Fig. 4. Spectrum of the Open Carbon Arc

The red rays, similar to those of the solar spectrum, were not detected with these exposures. However the additional short ultraviolets that extend to 220μμ are shown. Special carbons are used here. Ordinary carbon electrodes emit much fewer ultraviolet rays and these do not usually extend as low as 220μμ. Higher amperage is required.

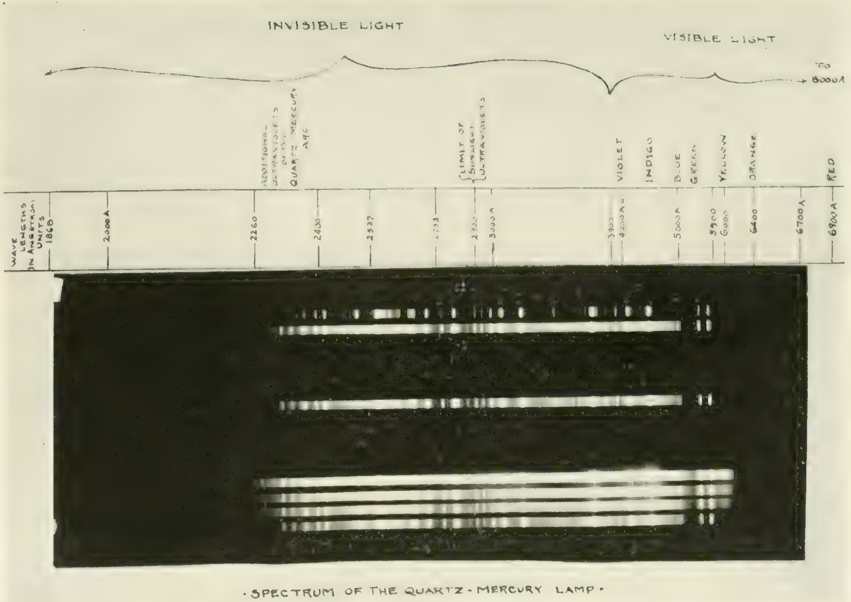


FIG. 5. SPECTRUM OF THE MERCURY QUARTZ LIGHT, SHOWING AGAIN ITS BAND TYPE, DISCONTINUOUS, WITH THE ADDITIONAL SHORT ULTRAVIOLET RAYS, DOWN TO ABOUT 226$\mu\mu$

In the manufacture of lamps, various types of glass have been used which are permeable to the ultraviolet ray, and are marketed as uran-glass, uviol-glass, cobalt-glass, blue-violet, tafel-glass, fluorite and rock crystal or quartz. Quartz and fluorite are permeable for the short ultra-violets, whereas the other glass is for the most part impermeable for those rays which are much below $300\mu\mu$.

The spectrum of a mercury quartz lamp, as found by Jüngling, showed one line in red, two in yellow and green, a strong one in violet at $436\mu\mu$, some few violets between $436\mu\mu$ and $400\mu\mu$, and then between $400\mu\mu$ and $290\mu\mu$ the following ultraviolets: $\mu\mu$ 390.8, 366.3, 365.4, 365.0, 334.1, 313.1, 312.6, 302.8, 302.3, 302.2, 296.7, 292.5. Beyond this there was an abundance of short ultraviolet rays from $292.5\mu\mu$ to 184.6μ.

From this we learn that the light is less rich in the longer ultraviolet rays, but contains an excessive amount of the short ones: the latter are the important rays to be considered in this lamp. There are very strong bands at $280\mu\mu$, $265\mu\mu$ and $248\mu\mu$. Uviol glass will let through to $250\mu\mu$. Depending upon the quality and the thickness of the glass, ordinary window glass will let through some long ultraviolets; but for the most part one can say that window glass is rather impermeable to them. It shuts out the short ultraviolets completely. An analysis of the mercury quartz light spectrum, as made for the United States Government, is shown in figure 5. This demonstrates its richness in the ultraviolet rays. The violet and blue rays are seen to be present also in fairly large numbers.

Jüngling compared with sunlight the various dosages that would bring about erythema. He found that with open sunlight, that which was obtained in fifteen minutes could be equalled by sunlight filtered through window glass (which let through the ultraviolets from $313\mu\mu$ upward) in forty-five minutes. With the quartz light open, the same erythema was obtained in one minute; and if this light was filtered with very fine object-carrying glass (microscopic cover slip) which let through from $280\mu\mu$ upward, the erythema occurred in ten minutes. Blue glass, if used, does not let in more violets and ultraviolets but eliminates the red end of spectrum. Workers have tried to obtain a filtered quartz light so that the patient could endure the exposures for a longer time if the short ultraviolets were eliminated; in this event they could then develop a better pigment without the irritating erythema. However, the types of glass that had to be used were too easily broken and eventually the chemical changes produced after long use rendered them unsuitable.

Finsen originally showed that the ultraviolets possessed very little penetrating power and were absorbed by the blood in the superficial vessels. By passing light through the ear, he was unable to obtain penetration of the ultraviolets unless he rendered the ear bloodless. The rays of long wave length, however, passed through. Russ could easily penetrate sections of the skin, cut from the human abdomen, with the ultraviolet rays. This he studied with the spectrograph. He also showed that rays from the Simpson light (Wolfram electrodes) are absorbed in 1.5 mm. of freshly cut human skin. Jansen and Bach found that the ultraviolet ray penetrated from 0.5 to 0.8 of a millimetre. Jansen tried to kill bacterial cultures through layers of skin and found that the shortest ultraviolets lost their power after penetrating thin layers. Nevertheless, in other experiments, some have felt that the short waves were able to penetrate living tissues, such as the cheek and hand, as demonstrated by Finsen, Busck and Lenkei. The latter two showed that the greatest penetration was possessed by the reds and infrareds. However, photographs were taken through a hand of about 3 cm. thickness with silver chloride plates (which were not sensitive to the heat rays).

Henri offers the following figures, showing the thickness of layers of protoplasm that absorb 90 per cent of the ultraviolet rays of different wave lengths:

Thickness of protoplasm in μ	79.0	58.0	18.0	9.0	6.0	3.8
Wave length in $\mu\mu$	240.5	238.5	231.3	226.5	219.5	214.4

To determine this, he employed as screens either euphos glass or colloidal solutions of silver. Euphos glass in a thickness of 0.75 mm. cuts off very little of the visible spectrum but allows only a small amount of the ultraviolets to pass through. Colloidal silver, in a thickness of 20 mm., allows no visible rays to pass, but is fairly transparent to ultraviolets as low as $210\mu\mu$.

Schmidt showed that the *red rays* were able to pass through very thick layers. Others have attempted to penetrate fatty tissue and muscle, and have found that whereas it took one second to penetrate the former, it required sixty seconds to penetrate the same thickness of the latter. Lenkei demonstrated that the *blue and yellow rays* penetrated tissues less than an inch; but in the absence of muscular tissue, the blue penetrated more than an inch. The yellow rays, in small amounts, penetrated almost three inches and the red rays had still greater penetrating powers. He found further that only 5 per cent of sunlight consisted of blue rays, whereas 80 per cent consisted of yellow and green. Schamberg was able to penetrate the tissues of the cheek and affect a photographic plate in the mouth, with the ray from an incandescent light intensified by a reflector. Busck succeeded in affecting a photographic plate through his hand with the red, orange and yellow rays in five seconds; but the blue and violets and ultraviolets did not affect it in ten minutes. Kime, Rollier and Malgat believe that they can show light passing through the thorax, forearm and hand. Gebhard demonstrated penetration through the palm with the electric arc. More recently, Gassul and Levy have reported on the deep penetration of the ultraviolet rays in white mice. They compared the ultraviolet light with the red light and could not obtain changes in the deep organs with the latter. The changes with the ultraviolets were an increased vascularity of the spleen and liver, increase of plasma cells in the splenic pulp, cellular infiltration and necrosis of the liver, and marked hyperemia of the kidneys. From this we see that the question of the exact penetration of the ultraviolet ray is still unsettled but the accepted opinion must yet prevail that *the penetration is very slight and does not go far beyond the superficial layers of the skin.* The works of Gassul and Levy are not very convincing as regards a deep penetration of these rays.

PHYSIOLOGY OF LIGHT RADIATION

There is so much diversity of opinion in regard to the changes in body physiology due to light, that the whole matter is not really clear. Some fairly complete studies have been made of the changes in the *blood cells.* Rollier has found with sunlight radiations an increase of the leucocytes, so that they average 10,000–13,000, an increase of the polymorphonuclear cells at the start, and then in cases with good prognosis an increase of lymphocytes. Red cells and hemoglobin were increased without sunlight exposures, due probably to the altitude change. The part that altitude plays must be taken into consideration in his results. Hyde, in the lowlands, has found increased red cells and hemoglobin and slight eosinophilia, with increased lymphocytes as the pigmentation progressed. Lenkei found an 8 per cent increase of erythrocytes, and 6 per cent of leucocytes. Von Schrötter claimed this was due to climatic influence. Others believe that the light rays, by destroying the superficial red cells, stimulated a compensatory overproduction of new erythrocytes. Increased concentration of the blood, resulting from sweating might also account for the change. D'Oelsnitz at Nice found a turn to the right in Arneth's formula in favorable cases: red cells and hemoglobin were also increased. Janet Clark more recently has determined the effect of the filtered light of different wave-lengths from an iron arc upon the blood cells of the rabbit. She found that the ultraviolet rays below $300\mu\mu$ can produce marked lymphocytosis lasting about three weeks, but have no effect on the absolute number of polymorphonuclear cells. The ultraviolets between $300\mu\mu$ and $390\mu\mu$ have a markedly depressing effect on the lymphocytes and to a less degree on the polymorphonuclear cells. The rays between $450\mu\mu$ and $650\mu\mu$ have a stimulating action on both lymphocytes and polymorphonuclears. The rays beyond $650\mu\mu$ have no effect. The erythrocytes remain unaffected with all rays for short exposures.

Berner concluded from his investigations upon patients treated with the mercury quartz light that there occurred no change in the red cells and hemoglobin but a decrease of the polymorphonuclear cells and a relative increase of the lymphocytes. He considered the drop in leucocytes analogous to the drop in lymphocytes when X-ray was employed. (Recently Russ, Chambers and Scott noted a marked drop in the lymphocytes of mice on exposure to very small doses of the X-ray.) Näcke, in employing the mercury quartz light, noted that immediately after exposure the polymorphonuclear cells in the peripheral blood as well as those in the part rayed were diminished. Somewhat later, however, the total leucocytes increased to a point higher than the count at the very beginning, and this in turn soon dropped to normal.

Löwenhardt found the very same changes in the red and white cells as Berner did. She further concluded that light, especially the blue light, increased the total quantity of blood. A suggestion was offered that the absence of any changes in the red cells and hemoglobin on the application of the mercury quartz light might be a false one, because of the drop in blood pressure. Higher blood pressure might give a greater count per cubic millimetre of blood.

Bardenheuer, at Leysin, found that solar exposures produced a lymphocytosis and a leucopenia; it seems, however, that altitude also played a part. Marti found in rats, kept in darkness sixteen days, a decrease of red cells and hemoglobin; this changed to an increase when they were exposed to the carbon arc. His findings are in contrast to many other reports but undoubtedly differences in technique account at least in part for the conflict. Mayer, of Davos, using rabbits and rats, found an erythrocytosis when the animals were kept in the dark (due to altitude, he believed) but the red cells did not reach their maximum as speedily as in those animals that were exposed to light. Bürke did not find an increase of the red cells or hemoglobin at a high altitude. Bering compressed the shaved ear of a mouse for four hours with a quartz lens attached to a mercury quartz light and obtained an increase of the red cells.

From the many opinions that have been offered, it seems quite difficult to dogmatically state the exact blood changes which altitude and light individually bring about, just as it is difficult to differentiate the changes brought about by the various regions of the spectrum. However, the majority opinion is in favor of altitude itself bringing about an increase of the red cells and hemoglobin, and that the drop in leucocytes, with a relative increase in lymphocytes, can well be due to the light rays; likewise, that lymphocytosis generally accompanies pigmentation; and finally that the absence of light will have little effect upon the red cells and hemoglobin, or that at least, if it does, it is rather a fleeting one. It is also probable that the longer ultraviolets and the dark violets should be given considerable credit for the blood changes, since the short ultraviolets are absorbed by very thin layers of skin.

Taylor examined 38 people who returned from a summer's vacation at Woods Hole, Massachusetts, and found an absolute increase of lymphocytes in 25 out of the 38, in accord with the development of pigment. Of the 13 with no increase, 2 failed to tan, 6 were so dark originally that it was impossible to determine an increase in the pigment, and 5 had a high count from the first. This lymphocytosis resembled the response of animals to small doses of X-ray, and was considered as possibly due to the effects of the ultraviolet ray. Taylor suggested the possibility of ultraviolet radiation acting directly upon the lymphoid tissue. This, of course, was pure hypothesis. During the stage of lymphocytosis in animals exposed to the X-ray, proliferation of the lymphoid tissue was found. At certain stages after splenectomy, and after the inoculation of cancerous tissue into cancer-immune animals, and following exposures to dry heat, an unexplained lymphocytosis has been found to develop (Murphy and Nakahara, Sturm, and others). Corper, however, could not verify this lymphocyte increase. The exact cause of these changes must yet be shown. Traugott, after ultraviolet radiations, found that there was no change in the number of red cells in man; but there was a uniform increase in the leucocytes, if the exposures lasted from ten to fifteen minutes. A similar increase obtained in the lymphocytes, as well as a more rapid coagulation of the blood and an increase in the number of blood platelets. The changes due to ultraviolet or X-ray or radium radiation upon blood outside the body are almost negative, so that all the blood variations found in vivo are hardly to be ascribed to a definite cause.

In studying the effects of an absence of light, Schoenenberger demonstrated that in blood counts made upon horses that had been for years confined in mines, and likewise in similar examinations made upon polar explorers who had been living for months in the polar nights, there was no change in the red cells and hemoglobin. Gudzent found that prolonged exposure to the ultraviolet rays increased the red cells and hemoglobin. Bering found this increase due to a thickening of the blood. He exposed white mice to artificial ultraviolet rays and found an increase of the red cells and hemoglobin after a three hours' exposure, but the white cells remained unchanged. Grober and Sempell found no anemia in 22 horses that had been in mines at a depth of 637 metres for from five to ten years. The red cells were slightly increased and the hemoglobin little decreased. Graffenberger, on the other hand, said that the absence of light diminished the hemoglobin and the total quantity of blood. Marti likewise maintained that he demonstrated in rats a decrease in the number of red cells and hemoglobin. Exposures of animals to the mercury quartz lamp have shown for some a definite increase in the red cells. Similarly, observations made during expeditions in the Egyptian desert have shown an increase of the red cells. This lack of uniformity in the blood changes may be due to differences in technique or variations in the time at which the blood was taken or variations in the periods of exposure. However, it does indicate that certain blood changes may occur, and this should stimulate further interest in the matter.

In a further consideration of effects upon the *blood*, Hertel found that under exposure to the ultraviolet rays a change occurred from oxyhemoglobin to reduced hemoglobin. Hasselbach found that with the rays under $310\mu\mu$, the lipoid membrane was dissolved and hemolysis occurred. Grober demonstrated that the ultraviolet rays were absorbed by the blood in large numbers; Bering and Meyer, that the ultraviolet rays increased the peroxidases of the blood; Quincke, that the cells of the blood took up oxygen more quickly in the light than in the dark. The ultraviolets therefore exhibited both an oxidizing and a reducing action.

As concerns *respiration* Hasselbach noted a change to slower and deeper breathing after exposures to the ultraviolet rays. With sunlight von Schrötter, Durigs and Zuntzs found decrease of alveolar CO_2, deeper respiration and increased ventilation. Lenkei noted deeper but faster breathing.

The *pulse* may or may not be affected. With ultraviolet radiation, it is usually unchanged. With sunlight there is generally an increased frequency. Augsten, after exposures to the ultraviolet light, found no change in the pulse and respiration, but there was a lowering of the *blood pressure.* The opinion is uniform that there is a diminution of blood pressure following light exposure, due to dilatation of the cutaneous vessels, or, according to von Schrötter, to a deep central effect.

The *urine* has been found by von Dohl, Dotzel and others to contain albumin after ultraviolet exposures; but this was eventually considered to be of orthostatic origin. Diuresis occasionally occurs.

Various changes, not uniform, occur in the *body temperature.* After exposure to sunlight, the skin temperature usually rises, and the deep temperature falls. However, if patients expose themselves to sunlight completely clothed, heat will be retained and the deep temperature will rise. In this case, likewise, blood pressure may increase. Lenkei saw both a fall and rise of rectal temperature; Ivanoff never observed febrile reactions. After ultraviolet exposures, the first effects are occasionally a slight rise in body temperature which is later followed by a fall. At times, in some patients with rather high fever, the ultraviolet exposures have gradually but consistently lowered the temperature. Levy found no uniform change in the body temperature while using the ultraviolet rays. There were various oscillations and an occasional subfebrile reaction, but no uniform results.

On the *nervous system* ultraviolet exposures frequently have a soothing effect; but at times patients become irritable and nervous. Some patients are able to sleep better after these radiations. The blue rays are supposed to have a soothing influence in contrast to the exciting effect set up by the red.

An *analgesic* effect is often seen, especially in intestinal cases or in painful arthritis, myositis and neuritis.

On the *vasomotor system* there is generally a stimulating effect. The superficial vessels are dilated, with an erythema produced by both the red rays and the ultraviolets. As a result there may be a temporary decongestion of the deep viscera. McCaskey has shown that with marked overexposures to the mercury arc, symptoms of shock, with exhaustion, low blood pressure, chilliness and fatigue set in.

Other work has shown that vitamines are not affected (Hess). Complement can be easily destroyed, but antibody and antigen are less easily affected. Variations in these changes occur, according to whether exposures are made to sunlight or the diffuse light of the laboratory or to ultraviolet rays. Hydrogen-ion concentration has shown no changes.

The effects upon the skin are most important:

Changes in the *histology* of the normal skin, after light exposures, have been variously studied; and the following phenomena have been found: A dilatation of the superficial and deep skin vessels; the epidermis loosened and vacuolated; exudate permeating the corium; marked division of the nuclei of the epithelial cells; a migration of leucocytes; and a dilatation of the lymph spaces. In certain persons, the repetition of such sunburn produces a chronic condition of pigmentation and excessive keratinization which may lead to a cancerous formation called *xeroderma pigmentosum.*

These changes were similarly studied in lupus; and there was demonstrated, in addition, vacuolar degeneration of the giant cells, which after repeated exposures finally caused their complete destruction, as well as degeneration of the epithelioid cells and round cells. The blood vessels are the first parts affected. There is a gradual swelling of the endothelial cells which finally occludes the vessels. The ultraviolet rays possess the chief destructive influence; and the epithelioid cells are especially susceptible to their action. An immediate erythema occurs after exposure of the normal skin to red rays, but a latent period exists before the formation of erythema from ultraviolet radiation.

Finsen placed the body of a tadpole in moistened filter paper and studied it microscopically when it was exposed to the sunlight. He was able to note a dilatation of the capillaries, slowing of the blood stream, a contraction of the red cells and a migration of leucocytes.

Various theories have been offered in reference to the power to stimulate the skin cells to send forth large numbers of antibodies. On this basis Moro's inunctions of tuberculin are supposed to give better results in treatment than the subcutaneous injection method. Similarly, Pandorff gives his tuberculin intracutaneously, believing that he thus obtains better results. Wichmann cites a case of lupus, which developed in the skin of the neck of a patient with tuberculous laryngitis. In this case rapid healing of the larynx occurred; from which he reasons that there was a rapid throwing out of antibodies from the skin where the lupus area developed. Of course, these are pure hypotheses and quite untenable.

Light is able to render the skin immune to infections. This was demonstrated in a variola epidemic at Leysin, in which no patient, who developed pigmentation under sunlight treatment, showed the skin eruption of variola, whereas all others in intimate association with the latter, but who were not pigmented, had severe eruptions.

Previously unradiated skin will show *three kinds of reaction* when exposed to sunlight:

1. *Heat erythema* appears after five or ten minutes as a spotted hyperemia, and this pure heat reaction can be obtained through any other heat-producing agent. It disappears, according to the duration and intensity of sunlight action, after a half to one hour.

2. The *light erythema* is hardly differentiable from a burn of the first degree, but it has a latent period lasting from three to six hours. The intensity depends upon the intensity and duration of the sunlight treatment. The erythema varies from the slightest pale pink to the fullest red.

3. *Pigmentation* shows from the second to the third day, the erythema lasting, according to its intensity, from three to six days. The red shows a yellowish undertone and after a while the pigmented skin may be exposed to intense sunlight for even a whole day.

The intensity of pigmentation obtained in high and low altitudes is alike. The fact that there is an absence of erythema in the skin that has been radiated several times proves that the skin possesses light-adapting properties. If radiation is interrupted, this adjustment keeps up for varying periods. Pigment in the course of weeks and months will become paler and at times, although less often, the pigmented skin peels off. If the skin is reradiated, erythema reappears after larger doses than those used on the unradiated skin.

The exposures that bring about erythema are considered by some as toxic doses of light, against which the organism protects itself by pigmentation. Rollier is strongly of this opinion, and he always tries to avoid redness.

THE NATURE OF PIGMENTATION

The endogenous pigments are of several kinds, the principal ones being first, those which are usually called the melanins and which give the color to the skin; secondly, those that directly or indirectly are derived from the blood hemoglobin, such as hematoidin and hemosiderin; and thirdly, those associated with the breaking down of tissue cells, and which are in a sense colored lipoids. Only those of the first group concern us. The origin and chemical nature of these are not fully understood. The opinions vary between (1) autogenous development from the epidermis; (2) derivation from coloring matter of the blood, by means of the melanoblasts which in turn give rise to melanin (the mesoderm gives origin to the melanoblasts); and (3) autolysis of albumin, forming tyrosin or similar substances, which when acted upon by oxidases develop melanin. The evidence seems to be against their origin from the blood constituents. The melanins are usually dark brown or black. They occur normally in greater abundance in races exposed to sun and wind. In response to exposure, they appear rapidly in the form of tan or freckles. They contain no iron but are rich in sulphur. Wieting and others have shown that melanin is formed in the epithelial cells, apparently from the nucleus. These cells (melanoblasts) hold the melanin for a while and at other times transfer it to the chromatophores, the wandering cells derived from connective tissue.

Ehrmann was firmly of the opinion that an extracellular building up of pigment had not been shown, but that pigment formation belonged to the melanoblasts, the material for the pigment coming from the coloring matter of the blood.

Meirowsky exposed scars to light and was able to pigment them. He therefore maintained that pigment was not related to the melanoblast because it did not exist in scars. He thought he proved that the mother substance of pigment was not hemoglobin but a nuclear material that colored red with pyronin. This was chemically like tyrosin. Ehrmann, on the other hand, could not pigment scars, and reasoned that this was due to an absence of melanoblasts.

Many workers have found a great deal of tyrosin together with melanin in such conditions as melanosarcoma, and are of the opinion that the melanin developed in the primary elements of the tumor under the influence of an enzyme which acted upon tyrosin and other decomposition products of proteins. They further believe that in Addison's disease the products of albumin, to which tyrosin belongs, could not be acted upon by the secretion of the adrenal gland, so that these remained in the epidermis as propigments and were acted upon by the many oxidases to form pigments.

According to Solger, pigment is increased first, by outside irritants, such as the ultraviolet ray, pressure, rubbing, or any inflammation; or secondly, by a reflex through the nervous system in such conditions as pregnancy, and in intoxications as syphilis, cancer, Addison's disease, bone disease, and tuberculosis.

Schmidt believed that he could follow the change of hemoglobin into pigment in the frog. Carnot verified this in his observations on the intestine of a leech. Finsen and Quincke followed this opinion in view of the fact that chromatophore substances were often found in the neighborhood of the skin vessels.

Bloch thinks that pigment occurs in the skin and hair through an enzymatic action, which brings about a process of oxidation and condensation. He considers the reaction specific and finds it only in layers of skin that have been excised from patients or animals who have the ability to form pigment. He is unable to obtain it in albinos. He adds dioxyphenylalanin (a tyrosin product) to the cut sections of skin and obtains a dark, diffuse or granular substance. He finds this only in ectodermal tissue.

These different theories of the development of pigment have not received common acceptance. The pigment that occurs under sunlight is a more permanent one than that developed under the ultraviolet rays. It is likewise of a redder hue. That which forms under the quartz light assumes a browner color. It is evident that the pigment which develops under light differs from that found in the negro, and of course we cannot conceive of any relationship between pigment and tuberculosis in this race.

A fairly permanent dark pigment is obtained by a combination of ultraviolet radiations with sunlight exposures.

There have been many theories offered as to the *functions of pigment.* The two most reasonable ones appear to be:

1. The pigment is merely a protection developed against an irritation such as the ultraviolet ray, so that it allows us to withstand large doses of light. Because of this the side of the body generally turned toward the light is more pigmented than the less exposed sides. The part of the body that lacks the protection of hair and clothes is likewise pigmented, and often the pigmentation is in proportion to the need.

2. Pigment is a sign of good response to an irritation. This seems to go hand in hand with the belief that patients developing good pigment generally fare better than those who lack pigment. Gauvain felt that

the prognosis in early tuberculosis for patients who formed pigment with difficulty was not so favorable as for those who had advanced disease but showed good pigment. Pigmentation does often occur correspondingly with improvement and if it has a direct relationship with lymphocytosis, it may guide us with regard to the problem of resistance in tuberculosis.

Other theories that have been mentioned are the following:

1. Pigment has the power to change short rays to longer and more penetrating ones.

2. The pigment itself is absorbed by the blood stream and acts specifically on distant foci.

3. Pigment changes the absorbed rays to living energy.

4. Pigment may act as a hindrance by preventing the necessary irritation which is desired. Rollier aims to develop strong pigmentation and to avoid erythema. Rost believes erythema is essential and purposely allows periods of depigmentation during his courses of treatment. Reyn and Ernst aimed to avoid pigment in their working with the carbon arc. Breiger could never be convinced that pigment had anything to do with healing. Morschein, in Leysin, saw no results in patients with pigment while in others he got surprisingly good results.

THE RESPONSE OF PROTOPLASM TO LIGHT

Most of our efforts have proved of little avail in teaching us the exact manner of the action of light; and, until we know more definitely how it affects protoplasm and the body physiology, we must rely chiefly upon empiricism. Then it may well be as Bovie says, "When we learn more concerning the relation between the organism and this imponderable part of its environment, radiations will find a place as therapeutic agents as secure as that now held by chemicals in rational scientific medicine."

Our cellular protoplasm has developed good adaptability to the heat and light of the solar spectrum but its mechanism is not understood. We realize that some components are more sensitive to light than others, especially when we consider the response in human vision. The absorption power of protoplasm increases as the wave-lengths of the ultraviolets decrease; it decreases as the roentgen rays decrease. Grotthus's law teaches us that only those rays are absorbed that are effective in producing chemical change, so that the greatest absorption is seen with the ultraviolets. Electromagnetic rays have no effect upon objects that do not vibrate in resonance with them. If the object vibrates resonantly and the light is completely absorbed in the surface layer, the ray is reflected; if the object upon which the ray falls produces friction when they meet, and if at the same time it vibrates with resonance, the rays are absorbed, temperature may increase, and the absorbed energy brings about chemical changes (Bovie).

In order to set a photochemical reaction in train, a certain amount of light energy is absorbed. The later stages may mean the continuance of the reaction depending upon a combined supply of light energy and resulting in a storage of energy, or the reaction may be one which proceeds of itself with the evolution of energy, but is accelerated by means of a catalyst produced by light. The catalyst may disappear and require to be formed by the continual action of light; or it may be more or less permanent and continue to act after the light is removed. Another class is that of coupled reactions in which the products of the light reaction are used up at once in another reaction with loss of energy.

The reaction of certain small animal organisms to ultraviolet light obeys definite laws. A minimum duration is necessary; there is a limit of intensity below which no reaction occurs, and the effect is independent of temperature. These facts point to the occurrence of a photochemical reaction whose products excite skin receptors.

The direct action of ultraviolet light on microörganisms and tissue cells is a destructive one. The shorter the wave-length, the more powerful the effect with equal energy of the radiation. (Bayliss.)

It has been clearly shown that the cell membrane can have its permeability markedly changed by light.

Bovie has attempted to study the action of the chemical rays on the unicellular paramecium, exposing it to ultraviolets of different wave-lengths, using first those at $160\mu\mu$ and later those around $200\mu\mu$. The former are strongly absorbed by the protoplasm of the cell and do not penetrate the nucleus, while the latter are strongly absorbed in the nucleus and but slightly absorbed by the protoplasm. With the former he was able to stimulate more rapid movements in the cell, following which it lost its powers of coördination and swam in circles. He was able to change the rate of cell division, even though he used such small exposures that there was no change in the motion of the organism. Cell division was always delayed; but, if short exposures were used, the delay was transitory and it was followed by an acceleration, so that the radiated organism had more cell divisions than the controls. Rays that are absorbed in the nucleus interfered with other metabolism and the animal finally died. Very short ultraviolets not present in sunlight have a higher absorption index in tissues than any of the solar rays, so that they can be absorbed by the pigment-forming cells of the skin, thereby destroying the latter.

If we knew the kinds of rays that a given tissue will absorb and the method of absorption, we might properly select suitable sources of radiation. Some active parts of protoplasm in certain light-sensitive organisms may be so altered by the changes produced by light that their chemical action will not be proportionate to the exposure. The shape or the mass of the tissues radiated may have varying influences. Also, small doses of radiation have a stimulating action upon tissues, large doses produce deferred physiological changes, while with still larger doses the latent period is very much shortened and made entirely to disappear, so that there is immediate death of the exposed tissues.

Various workers have attempted to explain the *chemical action of light*. Bovie ascribed it to the changes occurring in the unstable proteins of the cell. Neuberg, Bering and Meyer believed that an action upon the enzymes was responsible. Bering and Meyer studied the action of light upon ferments, and found that in the form through which it could pass through the skin of rabbits it had a favorable influence upon the peroxidases. They demonstrated that the action is more intense the nearer it approaches the short waves. The extreme ultraviolets, which were absorbed in the skin, have an absolutely inhibitory influence on these ferments. The blue-violets and inner ultraviolets, if applied in moderate doses, act favorably, but in larger doses are harmful. The red rays do not influence the peroxidases. The yellow, or even more, the green rays, with sufficient intensity, have a favorable influence. Hertel and Quincke ascribed the change to the splitting off of oxygen. Downs and Blunt believed it due to the oxidizing power of the rays. Schwarz considered it the result of the liberation of lecithins. Hoffmann and Schulz ascribed it to cholin, a decomposition product of the lecithins. Any change, physical or chemical, due to light acting upon protoplasm may produce physiological disturbances, but the changes depend upon whether the rays are absorbed and whether the absorbing substances are sensitive to light.

The relation of ultraviolet rays to lipoids is peculiar in that the rays sensitize them and prepare them for oxidation or fermentative decomposition. By facilitating the decomposition of the lipoids, an intracellular oxidation occurs without any additional oxygen from the outside. Ferments may thus be only secondarily affected by way of the altered lipoids which themselves acquire photochemical powers. The effects may at times be such as to confer a new impulse to tissue growth, or, because of the greater intensity, the tissues may be disintegrated and destroyed (MacCallum).

The very earliest changes produced by the radiation may not be extensive but the subsequent manifestations may be marked. We do not know what types of protoplasm are more easily influenced by light rays than others. When rays destroy part of the protoplasm and there is no recovery, the cell is unable to functionate and subsequent metabolism is interfered with, depending upon the particular activities which the cell has to undergo. Certain kinds of cells, and especially those that are rapidly dividing or are immature, are more susceptible to the action of the rays than others. As a rule, a dose is preferred above that needed to destroy diseased tissue, and yet not great enough to destroy the normal functions; but no absolute law can be laid down. Bovie, in emphasizing the above points, offers us some idea of the uncertainties still existing.

Wago has studied the effects of ultraviolet radiations on the cells of the cerebral cortex. It is generally believed that the action of the X-ray on the central nervous system is very slight; however, with the mercury quartz light the action is remarkably strong, resulting in swelling, atrophy, karyolysis and finally cellular death.

There are many other *theories in regard to the action of light* (with little to substantiate them):

1. Jesionek ascribes the good results obtained in disease of the deep viscera almost entirely to pigment. This he maintains can be carried by the blood like tuberculin and set up focal reactions.

2. Rollier is of the opinion that, aside from various metabolic changes set up by light, pigment is essential for improvement and has the power to change the short rays to longer and more penetrating ones. He based his theory on the work of the physiologist, Jena, who was able to cover the exposed parts of thermoelectric elements with carbon and thereby made the intensity of the ultraviolets such as to affect a galvanometer. This he believed was a possibility only if the ultraviolets produced heat.

3. Wichmann believed that the light stimulated the skin to send out great numbers of antibodies.

4. Others have tried to prove that the ultraviolets have a deep penetration.

5. Light acts directly upon the blood vessels and nerves of the skin, setting up a vasomotor stimulation, with increased oxygenation, and has a direct effect upon the tissue ferments.

6. Radiant energy, so called, the exact nature of which is not explained, is absorbed by the skin capillaries and carried to the depths.

7. Heusner offered the theory that light breaks down the skin proteins, these in turn acting as antigens.

8. Light does not influence the disease in any way but to help the patient psychically.

ACTION OF LIGHT UPON BACTERIA

According to our present knowledge, the bactericidal power of light rests chiefly with the blue, indigo, violet, ultrared and ultraviolet rays. The greatest power is possessed by the last-named. Finsen in his work upon lupus first aimed to destroy bacteria to cure the disease. It was demonstrated that many, but not all, of the bacilli were killed. Jansen showed that he could kill bacteria through skin at a depth of 1.5 mm., but that he was able only to diminish the virulence when they were at a depth of 4 mm. Mme. and V. Henri and Baroni showed that the rays emitted from a mercury quartz light caused tubercle bacilli to lose their acidfastness in a very few minutes and that death ensued in ten minutes. Rochaix and Colin, on the other hand, showed that Much granules were much more resistant. Strauss showed that in summer two hours' exposure on a clear day in the lowlands was sufficient to render cultures of tubercle bacilli sterile. Koch demonstrated that the tubercle bacillus was rapidly killed by direct sunlight but more slowly by diffuse daylight. Kattenbracher showed that in exposing cultures of tubercle bacilli to the rays from an iron arc for a period of five seconds up to sixty, there was a gradual diminution of the growth, whereas a similar growth exposed to ordinary light grew luxuriantly after forty-five seconds' exposure.

Siegert rayed lupus tissue and then inoculated the radiated tissue into guinea pigs, yet was able to infect the animals, showing that the bacilli were not all destroyed.

Bazzoni found that the destructive effects of ultraviolet light depended somewhat on its association with longer radiations. Isolated ultraviolet rays, even between $220\mu\mu$ and $250\mu\mu$, required several hours of exposure to kill bacteria very quickly.

The effect of light upon bacteria depends upon the quality and intensity of the light, its distance from the organisms, the period of raying, the temperature and amount of humidity, the moist or dry state of the bacteria, their number, the age of the culture, the species, the biological properties such as ferment and toxin production, and the power of movement of the organisms. Varying results have been mentioned by authors who exposed bacteria to sunlight. The time required for killing the organisms ranged from a few minutes up to two and one-half days. These differences depended upon the many ways in which the bacteria were exposed as well as the variations in altitude, time of the year, etc. Mitchell and Crough in 1900 were the first to compare the effects of sunlight upon bacteria in high altitudes and lowlands. Treskenskaja later compared the action of sunlight in the winter at Davos (height of 1560 metres) with the summer's sun at St. Petersburg (sea level) and found their action the same. She made the thinnest suspension of bacilli in peptone, and likewise with the thinnest layer of sputum rich in bacilli she found that at Davos bacilli are destroyed at the end of February in five hours, while in May and August it required only three hours. Furthermore, at sea level in the summer months, the bacilli were killed by sunlight in five hours; at a height of 900 metres in four hours; and at 1560 metres in three hours. Comparing these results with those obtained with dry heat, she found that the bacilli in pure culture laid out in the thinnest layer were still virulent after eighty hours' exposure to a dry heat of 65°–70°, although the virulence was somewhat diminished. In exposure to sunlight, she believed the heat played no definite part in her results.

Von Bergen in a more recent report from Leysin disagrees with Treskenskaja. His conclusions are: 1. The bactericidal effect of sunlight at 1360 metres, under the most favorable meteorological conditions, in the months from June to August, was manifested by death in one-half hour; in spring, and fall, one hour; in the winter, somewhat longer. On the coldest winter day, with least solar intensity, tubercle bacilli never withstood two hours' exposure. 2. The ultraviolet rays of summer sunlight from $280\mu\mu$ up, including the rays up to $450\mu\mu$, have only 20 per cent of the total bactericidal light effect. 3. The great variations in bactericidal power depend upon the geographical situation, weather conditions, etc., under which the experiment is held. 4. Maximal light and photometric effect go hand in hand with disinfecting power. The killing power is independent of the drying and heating effect of sunlight.

Momont and Neumark showed that bacteria in the dry state are more difficult to kill than when moist.

Dieudonné and Buchner, after absorbing the warm rays, showed that the bactericidal effect of sunlight still existed.

It is not exactly known how sunlight kills the bacilli, whether through oxidation, or coagulation or the splitting down of the albumin of living plasma. It is possibly by a direct effect on the bacterium itself, although action on the surrounding medium may play a part.

Thiele and Wolfe, working with the bacillus coli communis, found that the ultraviolets killed bacteria in the shortest time; the higher temperatures hastened the action; and the long rays influenced bacteria very little at room temperature but at higher temperatures they also were able to kill the organisms.

Wiesner, working with the typhoid bacillus and bacillus prodigiosus, came to the following conclusions:

> The number of bacteria has no influence upon the death of the germs. The changing resistance can depend upon the age of the bacteria, the greatest resistance being possessed by bacteria of 7–20 hours, with these remaining constant for a few days and then diminishing after that. Bacteria are less resistant in the dry state than in the moist. In the greater moisture of the atmosphere, bacteria die more slowly. An inability on the part of bacteria to obtain food during sunlight exposures causes them to die more quickly. The ultrareds and ultraviolets kill bacteria, one as strongly as the other. Higher outside temperature will increase light action; lower outside temperature will decrease the killing action. By intermittent raying the effect is the same as the sum of the rayings; the action of light begins with the moment of raying and stops the moment the raying is stopped. The chemical powers of bacteria are not weakened through light. Different groups of bacteria possess a varying resistance against light. The killing power of light can depend upon the intensity. Bacteria that have been first exposed to low intensities of light die faster than those that have not been previously exposed, if they are again radiated. Bacteria in watery media have not the property to flee from light but more often they go to it, this phototaxis being a physical tendency. The killing of bacteria occurs more speedily in the presence of oxygen than in its absence. The disinfecting work of sunlight is the result of direct harm to protoplasm. In free nature, sun disinfection may play an important part in preventing the epidemic and sporadic diseases.

Finsen found that concentrated sunlight killed the bacillus prodigiosus and typhoid bacilli fifteen times more rapidly than ordinary sunlight, and that the concentrated carbon arc was even more powerful. Bang showed that the carbon arc light of thirty amperes will kill a thin layer of tubercle bacilli at a distance of 30 cm. in six seconds. Henri found that while bacteria were killed in from fifteen to sixty-five seconds, there was no particular wave-length especially lethal, but that the effect increased more and more, the shorter the wave-length, testing as far as $214\mu\mu$. Hertel found that protozoa were killed in about the same length of time as bacteria. Tecon found that the disinfecting power of sunlight upon bacilli in sputum that was placed in sterilized sand, gravel and dust (in his experiments at Leysin) was absent in exposures of two to fifty-two hours; but when the sputum was laid upon beaten snow and exposed to sun, it was regularly rendered sterile in less than twenty-nine hours. The ultraviolet reflection from the snow undoubtedly played a part.

Downes and Blunt were the first to study this action of light as far back as 1877, but they did not realize the importance of the chemical end of the spectrum. They were later followed by Duclaux, Arloing, Roux and Tyndall, who showed that bacteria which were attenuated in virulence by light again regained their power when placed in darkness. Roux and Yersin later experimented with diphtheria cultures and came to similar conclusions. Diphtheria toxin loses its toxicity soon after exposure to the ultraviolet rays (five minutes) whereas diphtheria antitoxin is not affected in thirty minutes. Dieudonné also found that direct sunlight killed or attenuated bacteria. Afterward, Courmont and Nogier in 1909 studied the action of sunlight upon bacteria with much detailed labor. Cernovodeau and Henri found that in general bacteria varied in their sensitiveness to the ultraviolet rays, according to the variety. They also found that tetanus toxin was destroyed by ultraviolet radiations. Roux showed that, in the process of bacterial destruction, not only light but also the presence of oxygen was necessary. He found that anthrax spores were completely destroyed by light and air, but were not affected when air was excluded.

Wesbrook, repeating the work of Kitasato and a few others, to study the effects of sunlight on tetanus cultures, also found that oxygen was essential for bacterial destruction. Tetanus cultures were completely killed by sun and air; but he found it possible to stop at a point where pathogenesis vanished while life still remained in the spores. These spores on reinoculation into fresh tubes had their virulence even increased; but on inoculation into mice they were not found to produce any symptoms. This might have been due to a temporary attenuation or to the absence of the tetanus toxin or to the smallness of the dose,—the author was uncertain. Nogier showed that because of the peptones and albuminoids present in a bouillon culture filtrate, the tetanus toxin products must be diluted before radiation, if one expects to penetrate deeply enough to affect the substance.

Browning and Russ have demonstrated the marked difference in effect upon bacteria between the ultraviolets around $300\mu\mu$ and those at about $290\mu\mu$: there is a sudden sharp exhibition of bactericidal power by the latter. This also holds true for the effect upon proteins and probably accounts in most part for the added benefits obtained from the use of mercury quartz lights.

ARTIFICIAL SOURCES OF LIGHT

In a consideration of artificial light therapy, it is worth our while to take up in detail one of the first lamps utilized, namely the *Finsen lamp* (figure 6). This was a carbon arc of very high candle power with a special use of quartz lenses that were water-cooled to eliminate the heat. Lenses were employed, both to intensify the rays and to apply pressure directly upon the skin, so as to eliminate the blood that Finsen had found to be a barrier against penetration of the ultraviolet rays. Before Finsen, Widmark of Stockholm had shown that the skin inflammation, formerly thought to be due to the heat rays, was actually caused by the chemical rays, namely, the blue, violet, and ultraviolet rays. Finsen corroborated this opinion by allowing sunlight concentrated by lenses of rock crystal to fall upon the arm. He avoided burning by eliminating the ultrared rays, passing them through a layer of distilled water included between the rock crystal lenses and also partly by pouring cold water on his arm. Glass absorbs most of the ultraviolet rays, especially those of shorter wave-lengths; rock crystal allows them to pass through. The various parts of the spectrum were individually passed through rock crystal alone, or through rock crystal and a plate of blue or green or orange or red glass; and, although concentrated light was used, the red, yellow and green rays never brought on any inflammation. All blue and violet rays, however, did have this effect, which was found to be greatly increased by the addition of the ultraviolet rays. Finsen then treated cases of smallpox by eliminating the chemical end of the spectrum, believing that if the chemical rays could bring on inflammation in the healthy skin, it might increase an already existing inflammation. By this treatment he was able to prevent the formation of pustules in this disease. Svendsen definitely proved that light would change a vesicle into a pustule. He allowed his patients to enter daylight after the vesicles of the face were fully dried but those on the back of the hands were still moist. When the patients entered the light, the moist vesicles suppurated and left scars while no scars were left elsewhere. Bie, working with Finsen, was also able to show that the bactericidal power of the light resided almost exclusively in the blue and ultraviolet rays.

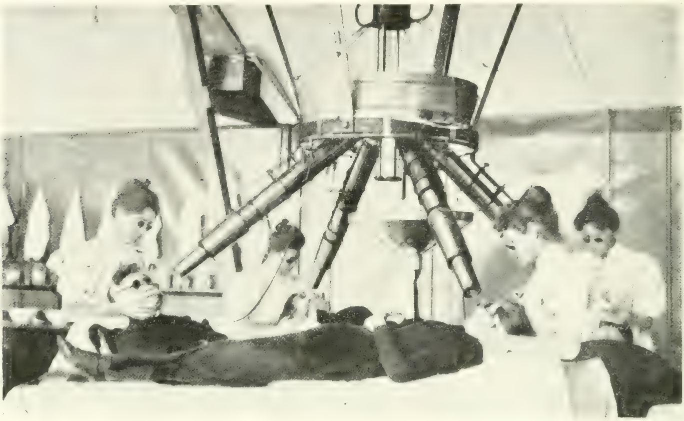


FIG. 6. A FINSEN CARBON ARC LIGHT, TREATING FOUR PATIENTS AT ONCE

The pressure lenses and watercooling devices can be seen. Lupus of the face is being radiated.

Accordingly, Finsen aimed to obtain light that was strongest in the blue and violets and ultraviolets, and had a minimum of heat rays, to avoid burning; he further desired to render the treated part bloodless, and tried to get the greatest concentration of the necessary rays. With *sunlight*, because of the large lens required, he was unable to use quartz, so that he had to resort to ordinary glass which partially allows ultraviolets to pass through from $380\mu\mu$ to $300\mu\mu$. The shorter ultraviolets are absorbed by both the atmosphere and glass. The *lens* (figure 7) used for sunlight consisted of a flat and a convex glass enclosed in a brass ring between which there was an ammoniacal solution of copper sulphate. This lens was preferable to a solid glass lens, because one surface of the fluid was arched and the other flat, so that it served as a planoconvex lens and not only concentrated but also cooled the light. Water absorbs the strongest heat rays (ultrareds), and by the addition of a blue coloring matter, part of the red, yellow and green rays are intercepted, which also possess considerable heat. The light is made just blue enough so that it cannot burn the patient.

With the carbon arc light, rock crystal lenses were used, enclosed in two brass tubes arranged like those of a telescope. The light becomes parallel within the brass tubes and at the lower end it encounters two lenses which bring the rays to a focus about 10 cm. from them. In the part of the apparatus between the last two lenses, there is distilled water which cools the light by cutting off the ultrared rays without absorbing any of the blue, violets and ultraviolets. There is a cap which encircles the lowest part of the apparatus through which cold water is made to flow so as to avoid too much heating of the distilled water. The distilled water is not colored blue because this would intercept part of the ultraviolet rays.

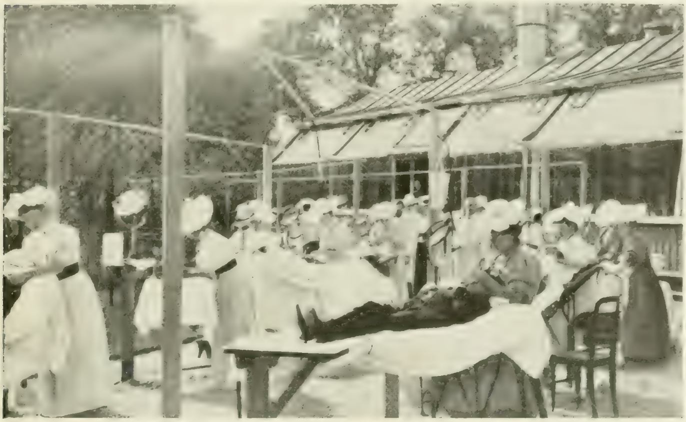


FIG. 7. FINSEN GLASS LENSES FOR APPLYING CONCENTRATED SUNLIGHT TO LUPUS

The watercooling attachments can be seen

Around each electric light there are hung four concentrating apparatuses on an iron ring which is held by iron supports made fast to the ceiling. The light although cooled is yet too hot to be directed upon the skin, so that Finsen devised a small apparatus consisting of a conical brass ring closed on both sides with rock crystal plates, one plane and the other planoconvex. The brass ring has an inlet and outlet tube filled with running cooled water, as well as four small metal arms, to which are attached rubber bands, so that the ring can be pressed against the skin to be treated. Besides cooling the surface, this apparatus expels the blood from the skin. Immediately after the treatment the skin is red and swollen, the inflammation often becoming so severe that a vesicle is formed but no necrosis results; finally scabbing occurs. Edema is occasionally seen. Lupus areas were exposed for about an hour every week for three to four months, depending upon the reaction. Pigmented areas or nodular granulations hindered healing.

I have entered into a description of Finsen's work with rather minute detail because it is upon his discoveries that most of the subsequent treatment with light was based. His results with lupus, the disease to which he mostly confined his efforts, were surprising. However, his apparatus proved too expensive and complicated.

The *mercury quartz lamp* (figure 8) consists of a quartz container supporting mercury vapor in a vacuum, through which an electric current is passed. An intense light is produced which is rich in violets and ultraviolets, with a preponderance of the very short ultraviolets. This lamp is an easy one to handle and the burners, if used carefully, have a rather long existence (2000 to 3000 hours). An objection to it is the expense of the apparatus. The life of the quartz container varies with the amount of usage. Deposits gradually occur in the quartz, finally rendering it impermeable for the rays. Bordier measured the strength of the quartz light with a blotting paper soaked in potassium ferrocyanide. The unit that he employed was the amount of ultraviolet ray that would affect a standard amount of silver nitrate in a given time. By determining the various changes that will occur in the radiated skin with the changes that have occurred in silver nitrate solutions so as to give him his standard units, one is able to judge the age of the burner. Schall tests ultraviolet radiation by using paper soaked in a solution of one gram of p-phenylene-diamine in 5 cc. of diluted nitric acid and dried rapidly in a Bunsen flame. The paper turns blue as a result of ultraviolet exposure. According to Shepard, in 1912, the Heraeus mercury quartz lamp offered the most intense source of ultraviolet radiation available. The photographs show several of the quartz mercury lamps sold in America; they vary slightly in construction. The air-cooled lamps are for general radiation.

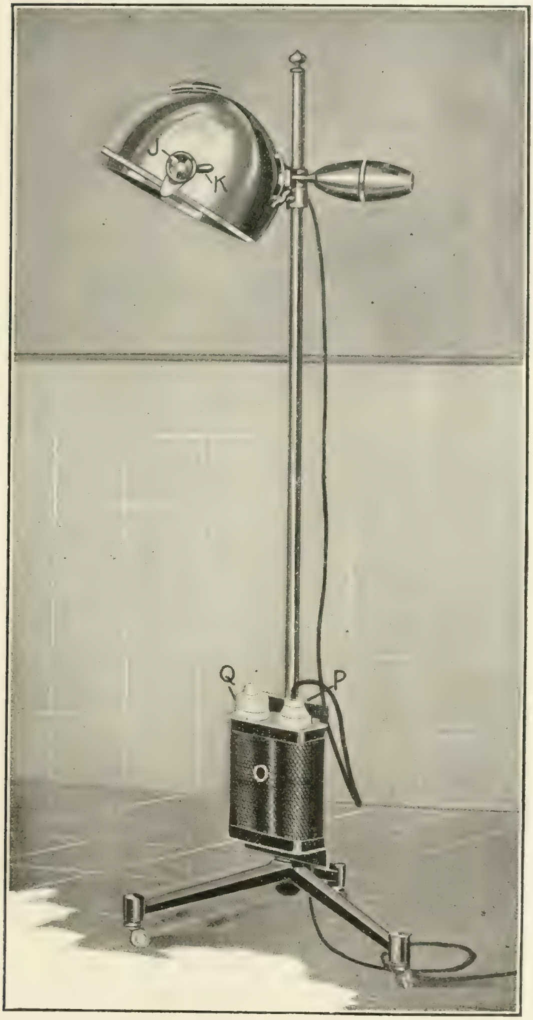


FIG. 8. THE ALPINE LAMP

An aircooled mercury quartz light, with aluminum reflector. Used for general applications.

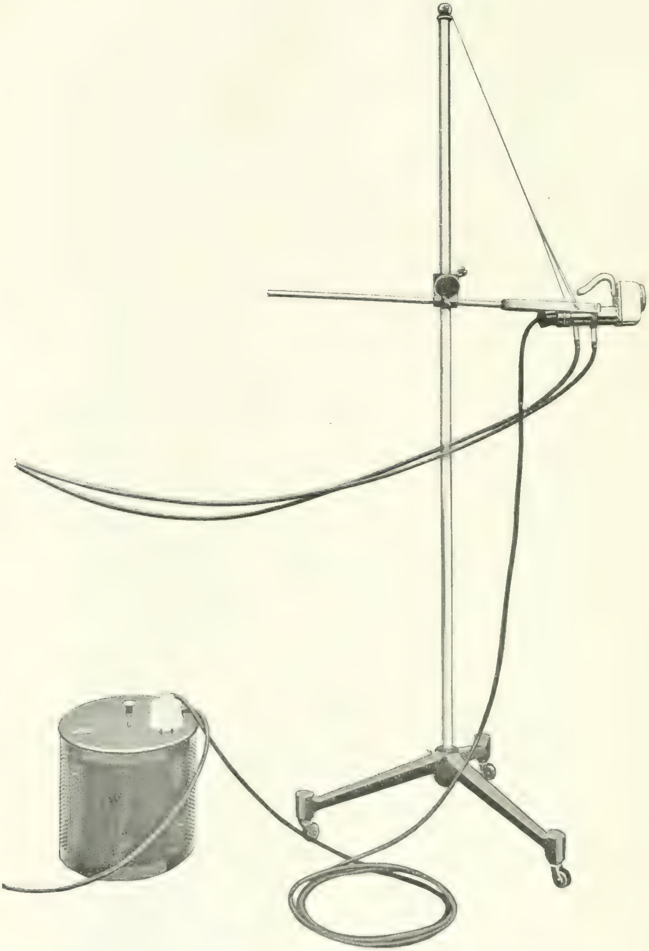


Fig. 9. The Kromayer Lamp

An intensified watercooled mercury quartz light, with pressure lenses. Used for local applications.

The *Kromayer lamp* (figure 9) is a water-cooled mercury quartz lamp used chiefly for local applications, and having special pressure lenses and other adaptors. It has an increased intensity of ultraviolet rays. The Burdick water-cooled lamp is similar to this (figure 10). The Burdick mercury quartz light requires a rectifier for alternating currents (figure 11). The Kromayer spectrum ends at 185$\mu\mu$.

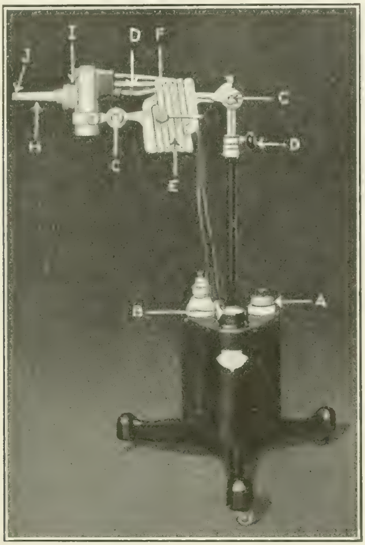


Fig. 10. The Burdick Watercooled Mercury Quartz Light, Similar to the Kromayer Lamp

Jesionek at Giessen has a large institute where his patients are able to stand or walk about or lie down during their exposures to the lamps. The rooms are specially equipped, so that the walls, ceilings and floors reflect the rays. The lamps shine upon the patients from the front and back and sides. The reflecting metal of the Jesionek lamp (figures 12 and 13) is an alloy of magnesium and aluminum, called magnalium. Four to six patients can take the treatment at one time. This lamp has also a mercury quartz burner.

The *uviol film lamp* consists of a mercury quartz burner surrounded by uviol glass to eliminate the irritating action of the short ultraviolet rays.

Other workers highly recommend the *open carbon arc lamp* (figure 14), marketed abroad as the aureol lamp. Schanz in particular praises this. He believes that the absence of the red rays and the abundant short ultraviolets of the mercury quartz light are hindrances. The additional red rays of the carbon arc, as shown by the spectrum in figure 3, are considered by some an added advantage in that the spectrum most resembles sunlight, but it is yet an open question as to whether the red ray is or is not necessary. The red end does produce an increased dilatation of the vessels and Schanz believes these rays necessary to sensitize tissues for a better absorption of the ultraviolets.

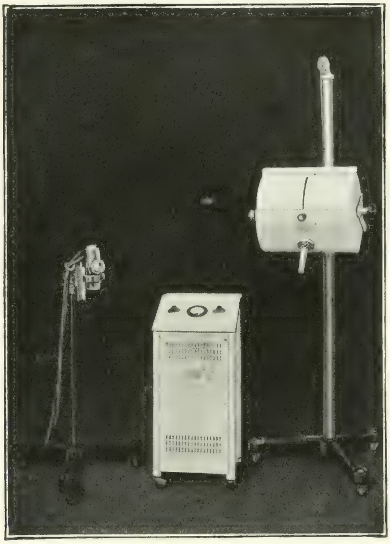


Fig. 11. The Burdick Mercury Quartz Light with Rectifier for Alternating Currents, Similar to the Alpine Lamp

The open carbon arc is much cheaper than the quartz lamp and is easily obtained in this country. Its electrodes are of carbon which soon burn out but then are simply replaced. The lamp flickers and throws out sparks and the carbons must be adjusted very often; but these

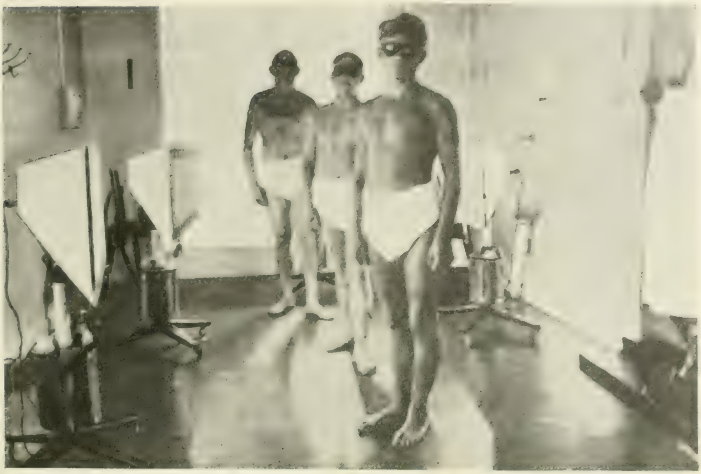


FIG. 12. PATIENTS EXPOSING THEMSELVES TO THE JESIONEK LAMPS IN ROOMS ESPECIALLY EQUIPPED FOR REFLECTION

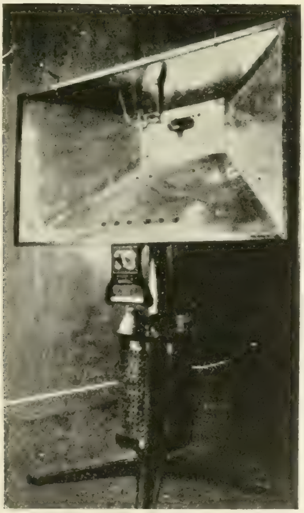


FIG. 13. A JESIONEK LAMP (MERCURY QUARTZ TYPE) SHOWING THE SPECIAL REFLECTOR MADE OF MAGNALIUM

annoyances are not great. It has additional heat which is absent from the quartz lamp. Intensified light is obtained by using strong parabolic reflectors.

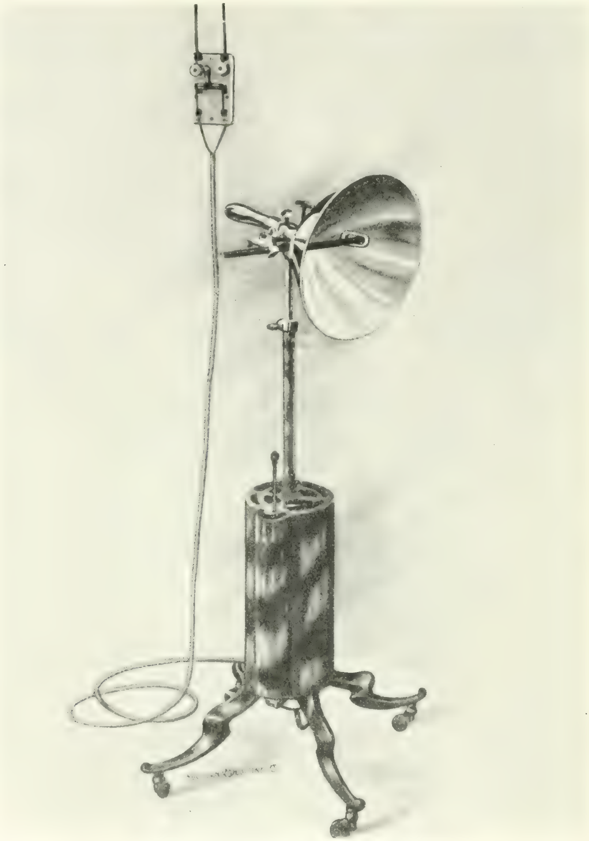


FIG. 14. AN OPEN CARBON ARC LAMP, WITH REFLECTOR AND RHEOSTAT

There are various types of this lamp on the market

Various other *metal arcs* have been used, especially in England. Among these are the Simpson light, with electrodes of the metal wolfram;

iron arcs that seem to give good ultraviolet radiation; and tungsten arcs, that have very high melting point, and are therefore especially recommended for ultraviolet radiation by Turrell. A large number of ultraviolet rays is given off by intensely heated iron, silver and copper. The iron arc has a greater intensity of ultraviolet rays than the quartz mercury light but it does not go as low in the spectrum. Other metal electrodes that have been used are zinc, nickel, cobalt, cadmium and magnesium. Some of them, especially cadmium, produce more uniform distribution throughout the entire range. Glass, mica, gelatin and even celluloid in very thin sheets are quite opaque to the ultraviolet rays, while quartz, fluorite and selenite are almost equally transparent to the visible and invisible rays. Christen employs a metal threaded lamp of the highest possible glowing temperature. It is surrounded by a glass that allows the ultraviolets to 290$\mu\mu$ to penetrate and this furnishes a spectrum that resembles that of sunlight. Roznowski used the Siemens aureol lamp, which is covered with glass, eliminating the short ultraviolet rays. It also has a spectrum like that of sunlight. An objection is that the glass breaks too easily.

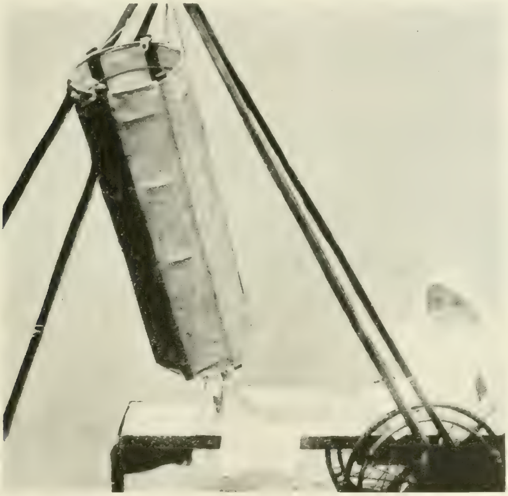


FIG. 15. THEZAC-POSMEUR APPARATUS, CONSISTING OF AN INTENSIFYING BICONVEX LENS MOUNTED INSIDE A CANVAS CYLINDER, AND SUPPORTED UPON A WOODEN TRIPOD

Schunck, Turrell and Russ, in England, give us much information on the relative intensities and therapeutic effects of the different parts of the spectra of the metal arcs. Schunck and Turrell favor the tungsten arc, when considered from the standpoint of ultraviolet content and resulting cutaneous erythema which can be thereby produced. Figure 16 affords good comparisons between the tungsten arc, iron arc, carbon arc and a Cooper Hewitt silicon mercury vapor lamp. The last differs somewhat from the spectrum of the Alpine mercury quartz lamp. The carbon arc, as shown here, is very poor in ultraviolets, but when special carbons are used, made up of impregnations or special cores, a good ultraviolet intensity can be had. Schunck has impregnated carbon with sodium tungstate and uranium nitrate, or put in special cores of tungsten powder or iron oxide or molybdium powder.

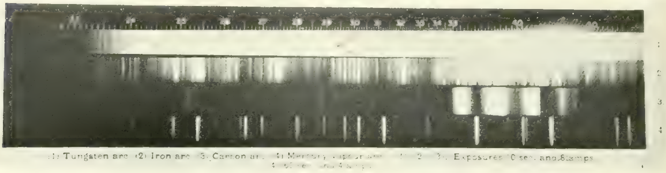

1
2
3
4
(1) Tungsten arc (2) Iron arc (3) Carbon arc (4) Mercury vapor arc
Exposures 10 sec. and 8 amps

FIG. 16. RESPECTIVE SPECTRA (BY SCHUNK) OF THE TUNGSTEN ARC, IRON ARC, CARBON ARC AND MERCURY VAPOR ARC

Note the quantity and intensity of ultraviolet rays in (1) and (2), to below 235$\mu\mu$. The carbon arc shows a maximum in a group of lines at 250$\mu\mu$, due to silicon. The mercury vapor is a Cooper Hewitt lamp of silicon glass, with a 110 volt lamp. The makers say that a 200 volt lamp should be used to get the maximum ultraviolet radiations from this source.

From various observations, Schunck found: (1) The iron arc reaches as low as 225$\mu\mu$ and shows a good intensity of ultraviolets but is not as uniform throughout as the tungsten arc. (2) The tungsten arc reaches lower (to 213$\mu\mu$) and gives the greatest ultraviolet intensity. (3) Molybdium reaches to 220$\mu\mu$, but has a lower intensity than iron and tungsten. (4) Wolfram (in the Simpson light) which consists chiefly of tungsten reaches to 213$\mu\mu$ and has almost the quantity of ultraviolets that tungsten has, but a marked objection is its unsteadiness. (5) The carbon arc is of low ultraviolet intensity, unless special carbons are employed. It requires higher amperage and longer duration. Its content of rays of the visible spectrum is of course high. (6) Uranium loses intensity at 260$\mu\mu$, but the lines are closer than tungsten and the spectrum more intense. (7) The Kromayer lamp reaches lower—to 1849 A. U., and has the greatest intensity around this low limit, just inside the Schumann region.

From his experimental work with the metal arcs, Schunck concluded that no therapeutic effect, as judged by the erythema produced, occurred from radiations of 2750 A. U. and upwards; that the greatest effect was produced by radiations between 2500 and 2350 A. U., with an increase in effectiveness from 2500 A. U. downwards. However, it seems impossible for one to judge only from the erythema produced and Russ has rightly questioned whether the rays between 2880 and 2960 A. U. were not equally effective as the lower ones from 2350 to 2500 A. U. Russ and Browning found a powerful germicidal action between 2960 and 2100 A. U., with a region of maximum effectiveness between 2800 and 2540 A. U. These rays were completely absorbed in 0.1 mm. of skin. Schumann found that the rays between 3000 and 2100 A. U. were easily absorbed by the human skin.

Some lamps furnishing only the red rays are also sold, one marketed as a neon light. An occasional worker like Gerhartz has given the red light treatment exclusively and believed that excellent results were obtained in treating tuberculous disease. Gerhartz treated advanced pulmonary and intestinal tuberculosis, following up his work also upon guinea pigs, but his results were rather indifferent, and surely far from remarkable. Nagelschmidt has made monochromatic lights, one liberating rays extending from the yellow far into the ultrareds, with a maximum of energy in the latter: another consists only of the red and yellow rays. The latter, called a neon lamp, emits a cold bright red light; the former, a hot reddish-yellow light. With the neon lamp he obtains excellent results with infected wounds and other superficial inflammations.

Artault de Vevey has written rather exhaustively of his treatments with what he terms the *heliophore*. This is a biconvex lens (of two sizes) mounted on a stand, and used to intensify the solar rays, concentrating them on small areas of the body. Its principle is somewhat similar to that of the lens of the Thezac-Posmeur apparatus, (which was introduced into America by Mrs. Post). However, the lens is smaller than the latter and is not so easily applied. The results obtained are due chiefly to the red end of the spectrum, although many of the violets and longer ultraviolets must also act. However, Artault is of the opinion that the red rays are most important. He has treated every type of tuberculosis but his enthusiastic claims must still be substantiated.

Lovett recently reported on the use of the Thezac-Posmeur apparatus, using it in cases of chronic suppuration, and found that the discharges were lessened, granulations assumed a healthier color, pain diminished, and an immediate lowering of the bacterial count was noted in the discharge. Hyde and Lo Grasso have also used it for a brief period and have thus far been favorably impressed.

In order to supply the lacking red rays, various workers employ additional lights together with the quartz lamp. Bacmeister supplies this heat with the sollux lamp, while Bach uses the mercury arc with additional glow lights. Hagemann adds a ring of incandescent electric lamps; this may also be supplied by some manufacturers. These lamps, on account of the warmth produced, often give the patients a sense of comfort, and by using only a certain number or those of varying candle power, any desired degree of heat can be produced.

Breiger has reviewed 124 publications appearing during the war. He found that 26 observers used natural sunlight, 54 the mercury quartz lamp, 8 the carbon arc light, 3 the red light, 7 the combined sunlight and mercury quartz light, 10 the combined mercury quartz light and carbon arc light, 2 the mercury quartz light combined with the X-ray, and 1 the glow light alone. This gives us some idea of the lamps in common use abroad.

HIGH ALTITUDES AND LOWLANDS

It is not our purpose to enter into the subject of climatology except in so far as it has to do with sunlight. Bernhard and Rollier mention the advantages of high altitudes as the following: An absence of moisture and other deposits in the atmosphere, little clouding, small amount of rainfall, dry snowy winters, summers not too hot, an absence of wind due to protection by peaks, air almost bacteria-free and dust-free throughout the winter and strong radioactive emanations which are even increased by the reflection of snow, and a resulting production in man of an increased number of red cells and hemoglobin and better circulatory powers with improved metabolism. Our interest in the increase of red cells is further stimulated by recent work performed upon aviators, which seems to verify these findings. Our former belief that the increase was due to a response on the part of the body to deficient oxygenation may have to be enlarged upon if one can prove a similar response to ultraviolet radiation.

After penetrating the atmosphere the intensity of sunlight (according to Langley) that remains in the lowlands is as follows:

	per cent		per cent
Ultraviolets	39	Yellow	63
Violets	42	Red	70
Blue	48	Infrared	76
Green and blue	54		

Von Violle says that at Mont Blanc the intensity of sunlight loses only 6 per cent in contrast to 20 per cent at sea level. The strength and duration of sunshine depends upon the clearness of the air, smaller losses occurring at higher altitudes. Dorno found that in the mountains the summer possessed the greatest warmth and the greatest ultraviolet intensity: following this, in order, the fall, spring, and least of all the winter. Bernhard says that next to the summer we have the greatest ultraviolet intensity in the spring, a fact that he believes is accounted for by the increased reflection brought about by the persisting snow.

The glacier burns occurring in Switzerland are seen much less often in winter than in summer. Schanz believed this was due to the short ultraviolets which may be present in the summer sunshine of a high altitude, but which are absent in winter. Bernhard is of the opinion that these burns are rarely seen in winter because none but the experienced skiers go about at that time, and they have already become accustomed to burns. Rosselet maintains that high altitudes have six times the ultraviolets of lowlands in winter, and twice as much in summer. Jüngling declares that there is no qualitative difference between low and high altitude sun. During the winter months the sun's spectrum differs from that during the summer months. He mentions that the shortest rays at noon in January are $307\mu\mu$ and in July $295\mu\mu$, showing that the extreme ultraviolets may not be necessary for therapeutic purposes. Freer does not find any variation in extent but only in intensity. The essential differences between low and high altitude sun consist to the smallest extent in the variations of the ultraviolet rays. Their intensity at low altitude drops considerably only in winter below that of high altitudes. In low altitudes the intensity in summer is greater than in winter.

Dorno carried out extensive investigations in Davos at an altitude of 1600 metres, studying the relative intensities of various regions of the spectrum at different times of the day, month and year. The intensity of the *warm rays* he found considerable throughout the year. A daily increase of about 25 per cent occurred up to noon. The greatest intensity was seen in March and April and the least in winter, but the maximum difference was only one-tenth of the total amount. Davos had 50 per cent more warmth than Potsdam but this was so divided over the entire year that extreme heat at high altitudes at any one time was not to be feared. The absolute maximum of Davos over Potsdam is only 10 per cent.

For the *light rays* (from the sun) there was an 80 per cent increase up to noon. Winter, spring and autumn have more than summer.

The *blue-violet rays* also increased 80 per cent up to noon, but in summer more than in winter. The greatest number exists in August and May, but a marked depression occurs in June and July.

The *ultraviolet rays* increased 450 per cent up to noon. The summer months (July, August and September) were the only ones that showed a large amount in the mornings and evenings. Dorno claims that in winter, even at noon, they possess very little intensity. Schanz disputes this point, considering Dorno's results inaccurate because he worked on the basis that there was a sharp differentiation between the visible and invisible spectrum. From these results, Dorno made the statements mentioned before, namely, that the ultraviolet rays are about twenty times as great in summer as in winter (at Davos) and that one summer day brought as many ultraviolets as a whole winter month. In contrast to the intensity of the warm rays, he found a decrease of ultraviolet intensity when the moisture of the air increased. The greatest ultraviolet intensity occurred on days that approached cloud formation or when the sky was lightly covered rather than perfectly clear. Intensity of light however will naturally diminish with the density of the clouds. This is in contradistinction to days on which the sun is but partly obscured by haze.

As to *total light* (which was considered as including sunlight and the "light from the sky") an increase occurred up to noon, in summer more than in winter; a maximum in July and May. The light reflex from the snowy mountains has considerable influence for six months of the year. With a blue sky, the sun averages 88½ per cent of the total light, whereas the diffuse light of the sky offers about 11½ per cent.

Clouds only slightly diminish the normal amount of light. The total daylight is increased by reflection. Dorno believes that in extreme cases the diffuse light can be increased through the reflex from the clouds as much as five times. Greater transparency of the atmosphere is seen at high altitudes. The clearer and more transparent the atmosphere, the more directly the sun works and the less the diffuse light works. In the lowlands, the diffuse light is greater and the difference therefore between the sun and the shadows is not nearly so marked.

As to the limits of the solar spectrum, Dorno's findings (previously considered) were not in accord with those of other writers. Those taken in Manila by Freer and those taken by Miethe and Lehmann in Assuan, Berlin, Zermett and Mount Rosa were practically identical, namely 291.5$\mu\mu$ to 291.2$\mu\mu$. They showed that altitude and lowland exhibited little difference in extent, although the intensity factor did vary greatly. Dorno noted 307.5$\mu\mu$ in January and 295$\mu\mu$ in July.

Duclaux found that the chemical effects of the solar light diminished in the summer months as one proceeded from a northern climate toward the equator (Algeria). However, the results obtained by Freer in Manila were contradictory to this, showing rather a marked increase.

As to the number of hours of sunshine, one is surprised to note the low figures for a place like Manila when compared with those of regions in northern climates. "Manila has 51 per cent of the theoretical sunshine as against 69 per cent for Denver and 76 per cent for Santa Fe. Even Chicago and New York present figures higher than Manila, namely 57 per cent for Chicago and 56 per cent for New York." Therefore, in considering the effects of the tropics, one must not lose sight of other factors besides sunlight. From experimental work carried out by Freer, he could not conclude that tropical sunlight contained a greater proportion of the shorter ultraviolets than the sunlight of northern climates; however, it did manifest a greater intensity of the longer ultraviolets.

When we realize the good results obtained by treating patients with surgical disease in the lowlands (results comparing favorably with those of Rollier have been frequently published, e.g., by Hyde and Lo Grasso in Perrysburg, New York, Bandelier and Röpke in Vienna and Cologne, Strauss in Eastern Europe, Vulpius in Middle Europe, etc.) and when we realize that the exposures there are carried on throughout the winter months, we must assume that the question of the intensity of the ultraviolet rays is not the deciding one. There seems no doubt that the ultraviolets in winter in the lowlands are much less intense than those at a high altitude; however, it is more likely that other factors of as great importance deserve their due credit. Finally, it is true that the shorter ultraviolets are not essential, although we cannot assert that their presence would not possibly aid.

THE AIR BATH

It is necessary to differentiate between the sun bath and what is ordinarily termed the air bath. The former requires a systematic exposure in the sun whereas the latter can be carried out in diffuse daylight, generally with a patient moving about, and carrying on slight muscular movements. The air bath, of course, may be taken while the sun is shining, but not necessarily so. The patient may strip or wear very light clothing, often just bathing trunks. The treatments last five to twenty minutes, according to conditions. In order to be able to carry on the muscular movements he must usually be in good condition.

Various workers use different indications, some requiring the patients to be afebrile and others considering this unnecessary. Liebe, more than anyone else, popularized this treatment abroad. The patient is graduated to the outdoor treatment and is eventually outside in all weathers except on rainy days, at which time he may take treatment in his room with the windows open. At the end of the treatments patients usually take cold baths and dry rubs. The general principle is one of vasomotor stimulation, and the various studies that have been made in regard to changes in the blood cells and body physiology show little difference from those made upon patients taking sunlight treatment.

The air bath is carried out continually as part of the hygienic cure in many of the institutions in Germany. Separate divisions of ground are graded and walled off for this treatment. Patients are carefully chosen and strict medical supervision is exercised. Overheating and fatigue are avoided. If the patient becomes chilled he must abruptly interrupt the treatment; if cool, he is given a brisk rub. All gymnastics, which are carefully advised, are stopped if the patient develops any pains (pleuritic) or dizziness. Friedländer advises this treatment for anemia, chlorosis, scrofula, neurasthenia and early pulmonary disease. Schröder limits these baths to quiescent pulmonary cases, of good nutrition, with no labile temperature, no fever and no cardiac disorder. Patients with pleurisy or tendency to hemoptyses or catarrh of the upper air passages are also excluded. Disease of the blood vessels or nervous system or kidneys contraindicate, when they accompany pulmonary disease, as well as marked weakness and nutritional disturbances. Contrary to Bandelier and Röpke, Schröder considers markedly anemic patients unsuited for this treatment. He found that the cutaneous vessels were first contracted and later dilated, that at first there was an increase of leucocytes and decrease of erythrocytes, followed soon by the very reverse. The blood pressure was increased, while pulse and respiration were slowed. Oxygen intake and carbon dioxide output were increased. Metabolism and the strength of the heart were increased.

Lenkei considered cool air baths essential, but felt that those carried out at a temperature of freezing in frost and snow were unnecessary. Many writers disagreed with Lenkei. Other studies have shown a rise of the skin temperature, whereas the rectal temperature drops in the first three-quarters of an hour and then rises. Winternitz found a rise in axillary temperature. Van Oordt found an increase of rectal temperature. Hemoglobin is increased; the viscosity of the blood first increases, then decreases; diuresis generally occurs. It is an important point for us to decide whether or not the good results claimed for sunlight treatment are not generally due to the possible effects supplied by the accompanying air bath rather than to any specific action from the sun's rays. This requires carefully controlled experiments.

METHODS OF EMPLOYING LIGHT EXPOSURES

1. Sunlight. In applying sunlight treatment, patients are gradually exposed outdoors as with the air baths, special care being taken to avoid any chilling or unnecessary exposures to winds. At the start, therefore, proper screening and protection from wind are essential. Rollier's method is a system of graduated exposures, beginning with a few minutes to the ankles and then daily adding another part of the body with a short exposure; but increasing the period of exposure of the part rayed on the previous day, so that eventually the whole body is exposed front and back for almost the entire day, especially in patients who develop a good pigmentation. The duration of the exposures varies with different workers. Malgat radiates for only twenty minutes; Bernhard three to four hours; Rollier two hours to almost all day; Szaboky one hour twice daily. The patient changes his position from time to time, and after the exposures, patients take cold sponge baths or shower baths and a brisk rubbing.

Malgat differentiates between a cold and warm sun bath, depending upon whether the thermometer registers an outside temperature below or above that of the body temperature. The cold bath constricts the blood vessels, lowers body temperature and raises blood pressure; the warm bath does the contrary. The periods of exposure vary according to the temperature. Patients are first radiated through closed windows; then outside in the open, first the back and after that the front of the chest, with additional reflected light on localized areas.

Practically the same method as that of Rollier is carried out at Perrysburg, New York. Pottenger, as well as Kime, in addition to general exposures, directs additional concentrated light upon the chest by means of a blue concave mirror. Flinn, in Arizona, avoids the chest in fever cases. Rollier, in his exposures for surgical cases, finds that he can avoid the use of braces but traction is applied in disease of the extremities. Open lesions are kept ventilated by the use of perforated dressings, so as to remain permanently exposed to the air. The head is preferably covered or kept out of the sun. In tuberculosis of the spine, postural treatment helps greatly to overcome curvatures (orthopedic surgical technique is otherwise adhered to).

2. *Artificial light.* In radiating with the lamp, various workers have refinements of application but they seem unnecessary. An easily applied method is to begin with an exposure of two minutes front and back, the quartz burner placed directly over the abdomen and lumbar region at a distance of three feet; and a safe rule to follow is to give daily radiations, increasing the period of exposure one minute every day, front and back. Many patients can then safely reach an exposure of one hour front and back. The necessity for stopping the exposures for a day or two can be determined by the response to the rays. If a severe burn occurs, one is compelled to advise longer intervals, which may especially be the case with blondes or red-haired patients. Brunettes often safely withstand exposures of two minutes' increase daily. The patient is most likely to obtain the greatest irritation during the earlier exposures. The lamp need not be brought nearer to the patient until an exposure of an hour's duration is reached, and then one can gradually diminish the distance to only eighteen inches between the patient and the quartz burner. An hour's radiation front and back may prove too long for some patients and if so one should stop much sooner. *The period of exposure from which one obtains the greatest benefit has not yet been accurately worked out.* There may be a point beyond which radiation can prevent good effects or even cause harm, especially because the short ultraviolets may destroy pigment in the process of being absorbed. Inasmuch as we are not certain of the exact depth of penetration of all the rays emitted here, it is safest not to place the burner directly over the thorax, especially in view of the uncertainty of the question of hemoptysis.

Other workers divide the body into halves, exposing the upper and then the lower half, front and back. This has an advantage in that it will probably cover more of the body surface, but then this requires rather direct exposures to the chest when treating the upper half. It is not necessary to follow out Rollier's method with the lamp.

The eyes should be carefully protected by glasses not made of quartz, as otherwise a severe conjunctivitis will be set up. It is sometimes advisable to cover the scalp because of a dryness and itching that may occur. Occasionally, itching of the skin or the formation of small blebs may cause one to discontinue the lamp for a few days. It is necessary to have the whole body as uniformly distant from the lamp as possible. The patients are able to carry out the radiations at home, if they can afford to hire the lamps for three month periods, as they are now rented.

Other workers will probably have individual methods which may be better than the one outlined. Some use two lamps front and back, having the patient stand or sit instead of lying down. Some men have exposed the chest directly to the quartz light, and claimed that there was no danger. If there is a superficial lesion in addition to the constitutional disease, extra radiations are given to the former. The dosage there applied is one that should aim at a good irritation,—enough to stimulate granulations rather than to destroy tissue. The duration of these exposures can only be determined by the type of lesion seen from day to day. If the Kromayer lamp with pressure lenses can be had, then one attempts direct pressure exposures to the superficial disease. At times the quartz light can be conveniently used in combination with sunlight radiation, a method that some men recommend highly.

The question of hemoptysis is one that may have to be considered, when applying direct exposures to the chest. We do not yet know the exact relationship, but some have reported such accidents.

Jesionek has his rooms so constructed with reflectors that his patients are able to go about as they please, not necessarily lying down; and, as a result, they do not tire of the treatment as easily as those using other methods. His is the more acceptable mode of exposure for ambulant patients but requires specially equipped rooms.

CONTRAINDICATIONS TO THE USE OF LIGHT

Various contraindications to the use of sunlight exposures in tuberculous patients have been advanced, although there is little uniformity of opinion in this regard. Schröder excludes those with accompanying cardiac disease, especially the obese, as well as the more irritable patients, and limits radiations to the fibrous form of lung disease. Others eliminate those in whom the tuberculosis is progressing, particularly those with high fever; and select only the stationary cases in good general condition. Still others avoid the following: Those who develop slight elevations of temperature; those in whom the pulse has a tendency to become rapid upon exposures; those who have insomnia; and those who show any signs of hyperthyroidism. Loss of appetite may prove an indication for discontinuance. Bacmeister excludes not only active cases but also all "open" tuberculosis.

Some accidental developments have been reported, as follows: Grawitz saw, under solar radiations, cardiac insufficiency and marked nervous irritability. Schröder observed tachycardia, high fever and an advance of the lung disease. Fever-free patients at times developed fever after the radiations. Bacmeister, Jacquerod and others found hemoptyses. Contrary to Schröder, the sun baths are recommended by Bandelier and Röpke and Liebe for obese patients. Liebe, however, is strongly against using them for patients with irritable nervous systems.

There are very few contraindications to exposure to the mercury quartz light, except for those patients who have a tendency to develop recurring headaches, nervousness and insomnia after radiation. There are a few in whom the temperature becomes elevated and, if this continues, it should be considered a contraindication. Some patients have a very sensitive skin and develop severe burns and large blebs, which may cause a discontinuance of the lamp.

The question of *hemoptysis* is one upon which workers do not all agree. With sunlight, Jacquerod maintains that hemorrhages frequently occur and therefore he is much opposed to its use. Pottenger believes that hemorrhage is not a contraindication. Morin at Leysin said that patients who formerly had frequent blood spitting, lost this tendency after employing solar radiation. In the report of the Massachusetts Tuberculosis Hospital, four hemorrhage cases that had been exposed to sunlight all did poorly. Bacmeister has seen hemorrhage occur in his patients who exposed themselves to sunlight with their clothes on and without regard to dosage. Certain workers claim that it is merely direct exposure to the chest that should be avoided. With the quartz lamp hemoptysis does not seem to be a contraindication, if we take the added precaution of avoiding direct exposures to the chest. Holmboe, who first excluded hemorrhage cases for his radiations, later exposed them and found no harm resulting. The writer saw two hemoptyses occur during exposures with the quartz lamp but no definite relation of cause and effect could be proved between the exposures and the hemorrhages: both patients had had other hemoptyses before using these direct exposures to the chest. Certain authors have even claimed that the lamp by bringing the blood to the skin surface may prevent hemoptysis.

EFFECT OF LIGHT UPON PULMONARY TUBERCULOSIS

1. Sunlight. In a consideration of the effect of light upon the various types of tuberculosis the most interesting and at the same time the most doubtful point is the question of its effect upon the lungs. There is no phase of the subject that is more disputed and upon which there is greater divergence of opinion. In Switzerland, sunlight was at first used rather extensively for pulmonary tuberculosis, but for the most part has now been discarded. Solaria that were first constructed for these cases have been discontinued. Jacquerod, who had over six years' experience with thousands of cases, as well as other physicians in Leysin, has discarded the treatment. They claim that bad results have occurred, such as activation of previously quiescent disease, as well as hemoptyses. Rollier, however, continues to use it in surgical cases that have concomitant pulmonary disease, selecting preferably those with no fever, in good condition and stationary signs. He mentions good results in second and third stage cases and suggests the possibility of an immunity developed in these cases by the surgical condition. Armand-Delille discredits sunlight exposures for pulmonary tuberculosis but employs them to prevent it after a pleurisy, or for tracheobronchial adenitis, with very satisfactory results in both cases. Malgat mentions excellent results; but he speaks much too enthusiastically of sunlight as a cure-all, and his work, it seems, would have to be substantiated. Morin also appears too enthusiastic. Renon and Szaboky have reported good results in afebrile patients. Haberling more cautiously offers his opinion that the good results were due to the climatic-rest cure rather than to radiations. Von Schrötter believed that sunlight had an important influence on pulmonary disease, but only indirectly.

Most workers agree that, by arresting glandular disease, sunlight is a prophylactic agent against pulmonary tuberculosis. It has been especially recommended for hilum tuberculosis in children, but less so in adults. Shortle has recommended it in pulmonary tuberculosis.

Pottenger believes that it is useful as an adjuvant, and exposes febrile patients. The Massachusetts Tuberculosis Hospital reports good results in 31 of 35 cases. Bacmeister cites cases in which the disease had definitely been reactivated by overexposures to sunlight. Webb and Gardiner have spoken of fair results in Colorado. At Perrysburg, New York, the pulmonary disease occasionally cleared up with the surgical condition.

2. *Artificial light.* Treatment of pulmonary tuberculous with *artificial light* has received considerable attention. Heusner has summarized most of the work abroad and concluded that fairly good results were obtained:—a lessening of cough and expectoration, a lowering of the temperature, an improved appetite, and a betterment of the physical signs. Breiger also noted beneficial results. Frischbier found that moist catarrhal cases became drier, with general betterment and loss of fever. Bacmeister uses the quartz light in conjunction with the X-ray, and feels that the former is an important constitutional aid in the treatment of pulmonary cases. Gustein reported rather steady improvement with quartz light exposures, but cautioned against overenthusiasm. Bochalli found subjective betterment in almost all cases but could find little objective improvement: in only one case was there a rise of temperature. Almost all of his patients enjoyed the treatment. Rubow and Wurtzen treated 16 ambulant cases with the carbon arc, always avoiding erythema, and obtained good results. Some authors recommend the use of the carbon arc, especially in cases in which a pulmonary collapse has been performed. Rohde carried out a rather unconvincing experiment, treating a few tuberculous guinea pigs with ultraviolet rays, and believed that he was able to cure those already diseased, as well as to prevent the development of the disease after inoculation.

Simon has given a brief report of his artificial light cases, and in this he speaks of exposures amounting to thirty-six hours in all. This does not seem a long enough period from which to expect results. Breiger, after an extensive experience, felt that he could not begin to obtain results until after a six or eight weeks' succession of radiations, by which time he had reached an hour's exposure front and back. Beyond a few contraindications previously mentioned, the lamp seems to be practically without danger for the pulmonary cases, but it has been rather difficult to select cases with a view to determine which ones may or may not be benefited by it. It is probable that brunettes do better than blondes, and it may be preferable to select well-nourished patients rather than emaciated ones; otherwise, criteria are lacking. If the result is psychic, then the most impressionable patient may benefit most. Since the dangers are so few, the lamp could be tried, if only for its psychic effect, in those cases that have already had a prolonged trial of routine hygienic-dietetic treatment and have not responded, regardless of the stage or activity of the disease. Under these conditions one has occasionally found rather decided improvement in some old chronic cases—even in those who have been having moderate fever, and in whom there have been noted loss of fever, gain in weight and restoration of appetite with improved digestion. However, if one entertains too high expectations, disappointments will be very frequent. It has seemed best to offer the treatment to patients as a possible rather than a probable benefit. Easier cough and freer expectoration have been observed although these symptoms were otherwise unchanged; bacilli in the sputum have been uninfluenced; physical signs of the chest have not varied.

Some patients have developed higher fever during treatment, which proved an indication to stop treatment. Likewise, an increase of other symptoms occasionally occurred and caused discontinuance. It is assuredly not a certain cure for pulmonary tuberculosis, but a good number of writers feel that it is an aid.

THE SIMILARITY OF FOCAL REACTIONS SET UP BY LIGHT AND TUBERCULIN

In the use of both artificial light and sunlight, one frequently notices at the beginning of treatment a slight rise of temperature with an increase of localizing pulmonary symptoms. This reaction has been likened by some observers to a tuberculin reaction. Jesionek believed that the pigment can act specifically, just as tuberculin does, and that, when carried by the blood stream, it sets up a focal reaction such as he has observed in the lungs, larynx and joints. These he obtained only in cases that developed good pigmentation. A latent period always existed before signs of the reaction appeared. He was able to cover his lupus areas by shutting them off entirely from the light, and then, by exposing the rest of the body, healed the diseased areas: he thereby apparently showed that something had to be carried by the blood to the focus. However, in his treatments he always preferred to expose the diseased parts, since he considered that the local inflammatory reactions obtained through direct radiations were very important. Rost also believed that he obtained better results in lupus if the lupus tissue itself was rayed, and maintained further that under general radiations he was able to observe small nodules develop in the bladder in tuberculosis of this organ, which he considered to be focal reactions. Grau similarly was of the opinion that he obtained focal reactions in the lungs. Englemann radiated the posterior part of a frog's body and observed changes in the retina. Schanz mentions an isolated instance of a tubercle upon the retina which disappeared under general radiation. Reyn and Strauss healed 30 cases of lupus, which had not been affected by local treatment alone, when they also applied general radiations.

ACTION OF LIGHT ON SURGICAL TUBERCULOSIS

1. Sunlight. By far the best results have been obtained with sunlight in this form of the disease, especially by Rollier in Leysin. Other reports comparing very favorably with those of Rollier have been mentioned by workers in the lowlands of America,—at Perrysburg, in particular.

Great benefits have been obtained from the treatment of *bones and joints* in which healing and a return of lost function occurred, together with rapid closure of sinuses. Peritonitis, pleurisy, and glandular and cutaneous tuberculosis have responded with almost equal success. Promising results have been seen in disease of the genitourinary and intestinal tracts, eyes, mouth and throat.

In Rollier's results the intensity of the ultraviolet ray is but a small factor. This must be so when we realize the benefits attained in the lowlands, even in winter. Evidently the good surgical technique and the ability to have patients remain under his care for prolonged periods play their part, and, furthermore, the stimulation due to the air bath must be a factor in increasing resistance. Hyde at Perrysburg, New York, noted a return of motion in joint cases only in the early stages, while with Rollier joints which had already undergone fibrous ankylosis had their function restored. Both workers found that muscles of the affected limb did not suffer atrophy during treatment. Hyde observed that sunlight usually reduced the amount of pus in abscess cases and frequently caused their complete absorption. Lymph nodes were gradually reduced in size, and in suppurating nodes there was an absorption of their contents. *Effusions* in joints, peritoneum and pleural cavity were also absorbed, but this was especially marked with the peritonitis cases. Lucas, in California, using solar therapy for peritonitis (when there is an excessive amount of fluid) found that better results were obtained when operation was carried out first, and then followed up with solar exposures after the distention was relieved. Rollier obtained better results in the closed forms of surgical tuberculosis than in the discharging cases. He noted frequent spontaneous absorption of glandular abscesses, so that he punctured only those which were about to break. Directly following solar treatment, the fistulae often became active and poured out their contents. The glands at times emptied themselves as "nuts from their shells." Wounds were protected by perforated metal coverings so as to allow air to get at them. If secretion was too great, the fistulae were covered with sterile compresses. In synovial disease healing is much slower. Conservative surgery was also employed by him in a rational way. Scherz carried out solar treatment for surgical tuberculosis in the lowlands. His results were very satisfactory in almost all cases. Operative interference was seldom needed. Kisch combined solar exposures with passive hyperemia and the internal administration of sodium iodide for the treatment of surgical tuberculosis. He reported excellent results. Severe tuberculosis of the joints was cured and function completely restored.

In *superficial tuberculosis* the question of proper dosage of light is an important one, small doses stimulating granulations while large doses are very liable to destroy them. This caution is not as essential with sunlight as with artificial light.

Steiner, reporting upon diseases in Java, has mentioned a lack of surgical tuberculosis in the tropics, and he assumed this to be due to the persistent sunshine. However, in the Philippines (as the writer has been informed) glandular and spinal tuberculosis are commonly seen.

In a consideration of the specific effect of sunlight upon tuberculosis, we must first know the action on *nontuberculous surgical disease.* Neuhof has worked along these lines in the treatment of fractures in rabbits, by placing some in sunshine and others out of it. He tested his results by the microscope, X-ray and tension, and found better and more rapid healing in those that were exposed to sunlight. This question should be investigated more extensively. In other nontuberculous conditions such as anemia, slow convalescence from diseases in general, rachitis, articular rheumatism, neuritis, neurasthenia, etc., rather enthusiastic claims have been advanced. Percy reported that in the treatment of fractures he had obtained better callus formation.

In *glandular tuberculosis*, Rollier reports from 85 to 100 per cent of cures in cases that did or did not have abscesses. Most results in the lowlands show little over 50 per cent cures. Results with X-ray treatment are better. The sunlight treatment of tracheobronchial tuberculosis in children is highly recommended. Armand-Delille, Lucas and others highly endorsed heliotherapy for children coming from tuberculous homes, especially for those showing positive tuberculin reactions or for those in whom one cannot definitely prove tuberculosis but who are nevertheless suspects, of poor nutrition and prone to develop respiratory complaints and possible slight elevations of temperature. In these the results, both from a curative and a preventive standpoint, are most encouraging. Chronic tracheobronchial adenitis is often present in these patients.

Strauss, in the lowlands of Eastern Europe, treated surgical tuberculosis with sunlight and found that with suppurating lesions he could not obtain the results that other workers claimed for high altitudes unless he first applied surgery and then followed with radiations. A few other observers have found this to be so and prefer radical excision first and then highly recommend sunlight for postoperative treatment.

In *genitourinary tuberculosis* Rollier reports healing 12 out of 31 cases; these were chiefly kidney and testicular disease. Rollier, Riviere and others found a rapid diminution of the pyuria and a marked relief of pain in cystitis, even if cure was not obtained. In *intestinal tuberculosis* Rollier reports 16 cases of ileocecal disease with 10 healed. An occasional isolated report, by Meyer, Rosselet, and others, of cases of intestinal tuberculosis that were cured clinically and had remained so for years after treatment, can be found.

In disease of the *skin* Finsen's results with lupus treated with intensified sunlight have already been considered. They were not as satisfactory as those obtained with artificial light.

In tuberculosis of the *larynx*, exposures have been carried out either generally or with the addition of local applications externally over the neck, or by direct reflection of sunlight into the larynx. There is a gradual tendency in this treatment toward increasing optimism, although there is far from uniformity of opinion. Sorgo, working with Rollier, reported good results with general exposures, while Forster and Mills speak very favorably of reflected sunlight applied directly into the larynx, A few reports from tuberculosis institutions have likewise mentioned promising results with general exposures. Jessen sensitized the tissues with eosin and then exposed to sunlight; his results were promising. Kunwald also advocated solar radiations for the larynx although Brünings experimentally could not prove that the procedure was worth while. Blumenfeld spoke discouragingly of his results. Jessen personally directed the reflected sunlight into the patient's larynx, for he believed the patient himself was unable to properly direct the rays upon the diseased tissues.

In tuberculosis of the *ears*, Rollier reports three cases cured by general solar radiations.

In disease of the *eyes*, Borel and others reported success, especially in conjunctival conditions. They mentioned the need of great care.

2. *Artificial light.* In consideration of the treatment of surgical tuberculosis with artificial light, we find that with few exceptions the lamps do not promise such good results, although in certain cases they may occasionally act as fair substitutes for sunlight. However for *superficial tuberculosis* the lamp may be more valuable, inasmuch as it contains the added irritating ultraviolets that set up better reactions and so respond more quickly with healing. Here one can also apply pressure lenses with the concentrated rays. The good results with lupus have been mentioned. The treatment of open wounds with the quartz light radiations, during the war period, appeared gratifying to certain workers only in those cases that had suppurated; clean wounds did not seem to be helped. From this one might conclude that the benefit derived was chiefly from the bactericidal effects of the rays. However, other writers have reported helpful stimulation of granulations and better cicatrization. This question must still be investigated. Ladebeck used what he terms a "quartz cleanser" which allowed him to cleanse deep areas of pus, mucus and cellular debris at the same time that he was applying the ultraviolet rays from the Kromayer lamp. It consists of quartz nozzles arranged so that sterile water flows during radiation.

In disease of the *intestines*, palliative results have been seen with the quartz mercury arc lamp, as evidenced by the cessation of abdominal pain and diarrhea, and a lowering or loss of fever. Frischbier, and Brühl have reported good results in the treatment of intestinal tuberculosis by this means; fever, pain, diarrhea and bacilli in stools disappeared.

Frischbier, reporting for the sanatorium Beelitz in 1917, says, "Especially remarkable was the favorable influence of the quartz light therapy on many cases of intestinal tuberculosis. Pain and diarrhea which had persisted for weeks, disappeared completely, as well as, in some cases, fever that had been lasting a long time; bacilli disappeared from the stools, the patients added weight, became ambulant, and felt stronger and better." How this occurs is still a matter for speculation. One cannot dogmatically exclude a direct effect on the focus, by possibly the violet rays (Frischbier applied the radiations to the abdomen), nor can one firmly assert that it is solely an indirect effect, brought about through the circulation. Other workers have seen benefits similar to those of Frischbier, but they apply the radiations to the whole body. This is a result that would make the quartz light very valuable, but experimentation along these lines is needed.

Recent communications on the treatment of intestinal tuberculosis with X-ray and radium radiations are also very encouraging.

In disease of the *bones and joints*, a moderate number of writers report excellent results with the lamps, some praising the carbon arc and others the mercury arc, etc. A few mentioned complete failures. In *peritonitis* excellent results have been obtained with a very rapid disappearance of fluid in some cases. Lacqueur and Lasser-Ritscher, employing the quartz light, treated 21 cases of tuberculous peritonitis, 12 of which were in children. They obtained a rapid disappearance of fluid in all but 6. The result was considered due to some immune substance carried by the blood. Budde also used the quartz light for peritonitis and also obtained good results.

In *tuboövarian* tuberculosis, Fromme speaks of 10 cases of pyosalpinx in which masses the size of a fist, which had been palpated, completely disappeared after comparatively few general exposures.

In *tuberculosis of the eye*, good results have been seen with general exposures in iritis and scrofula. Passow used the quartz lamp and the uviol lamp for this and mentioned good healing.

In *glandular* tuberculosis conflicting opinions are given but the majority report favorable results. More enthusiasm is shown, however, for X-ray treatment.

For the treatment of *laryngeal tuberculosis*, some indifferent reports have been made on the use of the "electric light" and the violet rays. With the ultraviolet rays, reflectors are now being employed, attached to the water-cooled quartz lights. This is a rather recent method and still in the experimental stage, with fair encouragement thus far.

Brünings experimentally radiated ulcerated tissues of the larynx with the quartz light, at the same time that he avoided overheating by a constant flow of water. In no instance was he convinced of scarring. On the other hand, he did believe that he could well demonstrate healing after treatment with roentgen rays; new connective tissue formation was seen but no real cure in an anatomic sense. He applied the X-rays internally and externally over the larynx. Fujinami obtained good results by treating lupus of the larynx with the Finsen lamp, both in the stages of infiltration and ulceration.

In treating superficial lesions such as tuberculosis of the larynx or mouth, or lupus of the skin, there is a question as to the exact manner of the action of the ultraviolet rays. Are all the results obtained in lupus due especially to the bactericidal effect of the rays, or to a direct, specific effect upon the diseased tissues, or to an inflammatory response to an irritation, which in turn stimulates the sluggish process? It is probable that all three factors play a part. A hindrance to the use of the reflected ultraviolet light may be the lack of sufficient intensity of the rays and the difficulty of direct application to the diseased tissues.

Blegvad has treated 52 cases of laryngeal tuberculosis with general exposures to the carbon arc, at times supplementing the treatment with the galvanocautery, and reports good success. Others speak of good improvement with the general exposures of the mercury arc.

Strandberg, Begtrup-Hansen, and Mälstrom, all Scandinavian writers, have been very favorably impressed with their results in the use of the carbon arc for tuberculous laryngitis, employing general radiations. However, their reports are chiefly impressions and not too convincing. Blegvad himself admits the need of the use of the galvanocautery in addition. Saugman, their countryman, said that the most effective treatment thus far for this complication was that of a sanatorium regimen. These writers all favor the carbon arc over the mercury quartz light, but they do admit the disadvantages of the excessive heat and fatigue which patients object to.

Heusner has reported a special light that he connects with the Kromayer and other lamps, consisting of a special quartz prism and mirrors. His impressions were also only favorable.

In tuberculous *otitis media*, Scheffer has made an encouraging report. By the direct application of the ultraviolet rays from the air-cooled quartz lamp, he was able to stop 4 chronic discharges in 5 patients treated. Pain was relieved once. However, we realize that many of these discharges stop spontaneously, so that it is hazardous to make dogmatic claims.

In *discharging sinuses* (including ischiorectal fistulae) local applications of fluorescent substances (dyes) in addition to radiations with ultraviolet rays have given indefinite results. Kirch mentions healing in some instances by this method, but Reyn could not be convinced of its efficacy. Nagelschmidt, by this procedure, was able to heal wounds in one-fourth the time otherwise required.

TREATMENT BY COMBINED ULTRAVIOLET AND X-RAY RADIATIONS

Bacmeister is strongly in favor of this combination for treatment. He uses ultraviolet exposures for their general constitutional effect and the X-ray directly for its effect upon the focus in the lung. He believes strongly in the ability of the ultraviolet ray to relieve pulmonary congestions; this may be aided at times by the addition of heat rays. The X-ray applied locally is used to stimulate the formation of granulation and scar tissue. It has not the ability to kill bacteria, as was shown by Küpferle and Bacmeister. In these cases they emphasize treating only the stationary types of tuberculosis and avoiding any progressive, destructive disease or even any case with merely a tendency to fever. With cases of surgical tuberculosis (glands, bones, joints, etc.) which are still in the infiltrative stage, X-ray treatment has given some excellent results. However, in the stage of suppuration, surgery must be resorted to. Bacmeister says, "Caseous glands belong to the surgeon; pus and sequestra must be eliminated by the surgeon; proliferating tissue should be rayed." In pulmonary disease he found that with very small doses of X-ray and prolonged intervals, little change appeared in the diseased tissues; very large doses in rapid sequence without sufficient reaction periods brought on bronchitis and bronchopneumonia, so that fairly large doses and sufficiently long intervals for reactions to set in and subside were found essential. This was shown to be necessary both in animal experiments and in human disease. Strong reactions were necessary in surgical tuberculosis, whereas these would be quite dangerous in pulmonary disease. Latent, stationary and slowly progressing forms of indurative disease of the lung responded well; pneumonic, exudative, or any acute destructive types were contraindications. His technique was to divide the diseased areas of the lungs anteriorly and posteriorly into small individual fields, as determined by the physical signs and X-ray. These fields were then radiated successively, front and back, with a dosage of 4 mm. filter, amount 10–15 x. For diseased hilum glands a somewhat larger dose, about 15–20 x, was given at each raying. The more fields exposed, the longer were the reaction intervals. The dose was at times made smaller if reactions were too severe.

Before and after the X-ray exposures, Bacmeister employed two quartz lamps, anteriorly and posteriorly, raying the exposed upper half of the body, beginning at a distance of about 3½ feet with a five-minute period and increasing the exposure every other day two minutes and diminishing the distance two inches until, after six exposures, fifteen minutes was reached at a distance of about 2½ feet. Together with both the ultra-violet and X-ray treatments, a strict hygienic-rest cure was carried out, the patients never being allowed more than a half-hour's walk three times a day.

Holzknecht, De la Camp, and others have also treated pulmonary tuberculosis with X-ray radiations with favorable results; each employs his individual technique. The question of the most desirable dosage is still unsettled.

The results although promising are not yet convincing enough to make one feel that it is the treatment of choice. The cases selected seem the more favorable in any event.

Strauss applied these combined radiations in both pulmonary and surgical cases, and obtained only fair results.

Diathermia has also been employed in combination with light radiations and has some enthusiastic supporters.

PHOTODYNAMIC SENSITIZATION

The experiments carried out have not led to very constructive results, although some of them may yet point the way to the explanation of rather important problems. The application of light is still but little understood, and innumerable problems present themselves. The exact mode of the working of light upon protoplasm is not known; likewise the differences with which various cells react to it. One of the most interesting and yet least understood of the workings of light comes under the province of photodynamics. Raab was the first to discover this action in 1898, and since that time a large amount of work has been done, with but meagre elucidation of the subject. Bering has given an excellent review of this work up to 1914. Sellards, in 1918, added some important contributions. Bovie, Brooks, and others are still working in this field. In view of its importance, it is necessary for us to consider the subject from several standpoints. The application of photodynamics to tuberculosis, although not very promising thus far, may eventually offer us some real advances when the changes are better understood.

In general, the term applies to the changed action of light upon substances in the presence of fluorescent bodies. However, there is first a possibility that undue emphasis has been put upon fluorescence, for the reaction may occur with substances that have such a small amount of fluorescence that it is not detected by the ordinary means or it may occur even with substances that do not fluoresce at all. Fluorescent substances are those which give off light of a color different from their own or from that of any part of the incident light when they are illuminated. The light which is given off is usually of greater wave-length than the applied light, and the best exciters of this are the violet and ultraviolet rays.

Certain necessary conditions hold, namely:

> (1) Substances producing photodynamic action are able to absorb light and to fluoresce although the photodynamic activity is not proportional to the degree of fluorescence. (2) Only that region of the spectrum is effective the wave-lengths of which are absorbed by fluorescent substances. The most effective rays are the actinic rays. The longer red and yellow waves are active for methylene blue, the green and blue for eosin, and the violet and ultraviolet for quinine. It is, however, even possible that some substances may produce this reaction with wave-lengths which are not absorbed. (3) The light emitted by a fluorescent body is in itself ineffective. The fluorescent substance must also come in contact with the material upon which it acts. (4) Oxygen is necessary for some of the effects produced by visible light, but not for ultraviolet rays, and may even be detrimental to the latter. There is little evidence that the fluorescent body is altered. (5) Acidity or alkalinity does not affect the reaction. (6) Blood serum generally inhibits photodynamic action. (Sellards.)

The fluorescent substances to be considered are many of the dyes, quinine, the bile salts, chlorophyl, ferric sulphate and derivatives of hemoglobin such as hematoporphyrin. The uranium salts are very fluorescent. By the skilful use of these photodynamic substances, sensitized tissues may be destroyed by light that is otherwise unable to affect the unsensitized tissues. Accordingly, the resultant longer waves of light may be used, which are able to penetrate deeper into the tissues.

Through work along these lines independent investigators have determined various changes upon protoplasm. The following striking results will indicate some of these unusual changes. Red blood cells when mixed with eosin will remain intact if the mixture is kept in darkness, but in daylight hemolysis occurs under conditions in which the light itself has no effect. Paramecia in the presence of a certain strength of acridin are killed in six minutes in direct sunlight; while, in darkness but in the same strength and mixture, they remain alive indefinitely. The presence of a ferment, such as invertase, increases the effectiveness of light, in the presence of a fluorescent substance, 400 times.

Complement of normal serum is easily destroyed by short ultraviolet rays artificially produced. Longer exposures to direct sunlight will also render it inactive, even without the aid of fluorescent substances. Under ordinary laboratory conditions, diffuse light alone does not inactivate the complement in a few hours.

Amboceptors are found to be fairly resistant to photodynamic action. The bactericidal action of dyes when mixed with culture media is distinctly increased when exposed to the action of light. The enzymes and the toxins and antitoxins of diphtheria are rendered more susceptible to light by the presence of fluorescent bodies.

Jodlbauer injected a lymph sac in the posterior part of a frog's throat with erythrosin and following this the tongue was exposed to the arc light. In a few minutes the exposed part showed swelling, dilatation of the blood vessels and a clotting of the capillaries, whereas the unexposed part remained normal.

We may also meet with paradoxical situations. Thus, in conditions of jaundice in man, which implies the presence of bile pigments in the blood, there is no clinical evidence that suggests photodynamic action, although these bile pigments are active as such *in vitro*. Likewise hematoporphyrin will exhibit strong effects both in the test tube and in lower animals, whereas in conditions such as hematoporphyrinuria it does not usually lead to the production of definite symptoms in man. When found in the urine, it may be associated with cutaneous eruptions, but not always so. On the other hand, hemoglobin, freshly prepared and injected, can affect man to a great extent but is relatively nontoxic for animals. Hemoglobin in the blood has a protective action against the effect of light, the red cells protecting the serum and other components of the blood from the actinic solar rays. The red cells, as experimentally shown by Sellards, have considerable stability against light. Hausmann found that the bile pigments would produce hemolysis *in vitro* only in the presence of light. Sellards obtained hemolysis in sunlight by the addition of bilirubin to red cells, whereas no hemolysis occurred in the dark. Likewise, in the light, bilirubin prevented clotting in a few cases although it did not exert this effect in the dark.

Hausmann tried to produce hemolysis of the red cells experimentally *in vitro*; and was able to do so easily after exposure to the violet rays but only slightly so with the red rays. He was unable to obtain it *in vivo*. Sellards found a trace of hemolysis caused by the action of sunlight alone.

Some of the phenomena produced *in vitro* can be similarly produced in animals, showing that fluorescent substances may prove poisonous for animals which are kept in the light, but not for those kept in total darkness. Buckwheat poisoning in animals has been considered by many as due to photodynamic action, although others ascribe it to anaphylaxis. What follows here is, that when buckwheat is fed to sheep or swine, and if the animals are white or have white spots and are exposed to sunlight, serious symptoms develop; while if the animals are not exposed to the light the symptoms do not occur. Likewise, after their development these symptoms may subside when the animals return to darkness or even when the hair is artificially colored. Under exactly the same conditions animals that are dark in color will remain well.

White mice, fed with eosin and kept fourteen days in darkness, when exposed to sunlight die in one-half hour; if they remain in darkness, no symptoms develop. Mice that had been injected with eosin by Raab showed on exposure to light a necrosis of the ears and later died. Prime fed epileptics eosin (containing 47 per cent bromine) and, when exposed to sunlight, erythema with swelling and necrosis developed on the face and hands; this might well have been a photodynamic effect. Myer-Betz inoculated himself with hematoporphyrin and on exposure to sunlight developed severe symptoms. Raubitschek considered pellagra as a similar manifestation, attributing it to a substance which is obtained in corn, and which is active in the presence of light. He believed that he could produce the condition experimentally in animals fed on corn and then exposed to sunlight; likewise, that he could prevent it if the animals were kept in the dark, or if the diet were changed when the animals were kept in the sunlight. He even extracted an oil from the corn which produced similar effects. Brandenburg also believed that pellagrous patients were sensitized to light by eating maize, and that in this way light action became harmful.

Amsler and Pick have been able to bring about complete stoppage of the isolated heart, by perfusing it with solutions containing fluorescent substances, and then making exposures to light; this was due to an effect upon the nervous part of the heart rather than upon the muscle. In darkness, the heart continued to beat. Jodlbauer and Tappeiner have carried out innumerable experiments upon bacteria, enzymes, toxins, tissues, etc., with photodynamic sensitization, but finally believed that little encouragement could be offered in this field.

Reasoning that quinine is fluorescent, some authors have placed their malarial patients in sunlight. Viale claimed rapid improvement in 6 cases of long-rebellious malaria by just such treatment. Reinhard found malarial parasites in a much shorter time in the superficial blood vessels when he rayed the whole body with the quartz light, and employed a blue filter. He found this procedure valuable both for diagnosis and treatment. However, Sellards could not obtain *in vitro* any increased effect of quinine when sunlight was used. No evidence was obtained by him that quinine was dependent on its photodynamic effects for its action against the malarial organisms. Neuberg and others believed that in certain water cures the mineral substances acted as sensitizers of the body to light, so that it was actually a light therapy.

A few workers have attempted to use therapeutically this photodynamic action, but both experimentally and otherwise many obstacles seem to arise, so that for the most part only indifferent results have been obtained. It may be that when many phases of the subject are better understood, and more experiments are carried out and with better controls, we will obtain some satisfactory benefits.

Hofer, working upon cutaneous diseases of fish, employed eosin with exposures to light, and was able to destroy the skin parasites.

Jesionek and Tappeiner treated superficial tuberculosis with results that were not very promising. The results of Reyn were also unsatisfactory. Mayer, of Berlin, as well as Kirch and Nagelschmidt, applied dyes to suppurating wounds and then exposed the latter to the ultraviolet rays. Their results were very gratifying.

It has been found that protective action against infecting agents can only be obtained when the injections of the agent and the fluorescent substance are made simultaneously, and sometimes they are required to be made in the very same area. As a result we find striking differences between the test tube reactions and direct experimental results.

Although from the foregoing consideration of this phase of light action the therapeutic results have not been promising, further attempts along these lines are still being made.

SOME ADDITIONAL EXPERIMENTAL EFFECTS OF LIGHT

The question of the action of light upon proteins has been experimentally considered. Schanz has exposed the albumen of the lens of the eye, egg albumen, and serum albumen, and found that with ultraviolet rays he could change soluble proteins to less soluble ones. He further radiated organic substances such as acetone and formaldehyde and was able to break them up into their elements and radicles. Tuberculin was exposed to the rays from the mercury quartz light, and found after a sufficiently long period to lose markedly its power to cause the intracutaneous tuberculin reactions. At times this power was lost completely. The intracutaneous tuberculin test was frequently lessened in extent, when the inoculated area was exposed to the ultraviolet rays either before or after inoculation. The subcutaneous tuberculin reaction was found by Hoffmann to be markedly hastened in the presence of light. It appeared earlier after morning inoculations than after those given at night. The beginning of fever exhibited generally a six hour difference. This was worked out on the basis of a large series of tests in many institutes. Karczag studied the effect of sunlight on the allergy of albino and pigmented guinea pigs and found that there was a definite increase. Römer noted differences in the skin reactions between white and pigmented guinea pigs. Although Schanz believed that an opacity of the lens of the eye was developed after prolonged ultraviolet exposures, Burge did not obtain it even after one hundred hours of consecutive exposures to the quartz light.

Martin found that the cornea absorbed all rays shorter than $295\mu\mu$, but that the lens can absorb the rays between $300\mu\mu$ and $400\mu\mu$. The unmodified lens proteins do not coagulate on exposure to the short ultraviolet rays, while the serum proteins do. There may be some unknown protective provision present in the lens and in the humors of the eye, but if solutions of calcium chloride or sodium silicate or dextrose are added coagulation occurs. Birch-Hirschfeld believed that the ultraviolet rays could cause a cataract. Bovie found that the photoinstability of egg albumen and certain amino acids increased sharply as we pass from the ultraviolet of sunlight into the region beyond. Henri also showed that the extinction coefficient of egg albumen and blood serum increased many times as we passed beyond this region.

Müller reported on the influence of radiations upon reactions to the various partial antigens. He found that sunlight increased the whole partial reactivity but especially the albumin; X-ray increased the fatty acid lipoid reactivity; quartz mercury light increased the nastin reactivity.

Metals have been applied locally to superficial tuberculosis in combination with treatment with sunlight exposure. Thedering applied copper for treating lupus and reported favorable results. Schröder used injections of gold and thought he obtained some promising benefits. Hufnagel injected aniline into animals and this with sunlight exposures he believed caused a healing of the skin lesions. He also fed benzol to his tuberculous patients and exposed them to sunlight, and became convinced of the value of this procedure.

Baroni and Mihaiesti found that radiated horse serum could be injected into an actively anaphylactized guinea pig without injury; however, its relation to precipitable substances experienced no weakening, but on the contrary, an increase. A very long radiation of horse serum leads to the destruction of the specific precipitability with which the sensitizing property also experiences a reduction at the same time.

Doerr and Moldovan found that with normal sera the specific precipitability and the anaphylactic properties disappear; that with antisera, the precipitable as well as the passive anaphylactic properties disappear; and that the weakening of the antigenic qualities of normal sera and the immune functions of the immune sera for precipitation and anaphylactic reaction follows sufficiently regularly. Both authors could show the symptoms of antianaphylaxis by reinjection of radiated serum in anaphylactized animals, from which they concluded that, under certain conditions, corresponding to traces of precipitation, antigen remnants were held in the radiated serum (Wagner).

On the whole the experimental work has thus far not rendered much aid in the way of advance in treatment but the whole subject offers a field for what would appear to be some fruitful endeavors.

CONCLUSIONS

It is evident that we have yet many problems to solve. Some of these are: (1) The question of the exact mode of the formation of *pigment* and the actual rôle of this substance. (2) The proof of any specific powers possessed by pigment. (3) The ability or inability of pigment to change short rays to longer and more penetrating ones. (4) The relation of pigment to prognosis and lymphocytosis. (5) The ability of pigment to set up focal reactions in tuberculosis.

We require many more experiments to show the exact *penetrating powers* of the various rays, and additional data in relation particularly to the effect of violet and ultraviolet rays upon tissues, both healthy and diseased, and upon bacteria especially *in vivo*.

More experiments are needed to compare the effects of the ultraviolet rays with those of the red and ultrared rays, and many more comparative results between high and lower altitudes are necessary.

From clinical experience with surgical tuberculosis, evidence points to the greater value of the ultraviolet rays although it appears that the heat rays may also aid.

Insufficient comparative and statistical studies upon patients, especially upon those with pulmonary disease, leave much to be desired.

Much more knowledge must be had experimentally of the effect of light upon *nontuberculous* conditions.

In *surgical tuberculosis* we can conclude that with *sunlight* excellent results have been obtained with children in the treatment of bone, joint, skin and peritoneal disease. However, it seems better, especially in the lowlands, to remove debris (pus, sequestra, etc.) first and then apply radiations. In disease of the genitourinary tract, eyes and larynx, only occasionally favorable results have been had. General exposures have given only slight and doubtful improvement in laryngeal tuberculosis. Local laryngeal exposures by means of reflected sunlight may eventually accomplish more for us.

With *sunlight*, *intestinal tuberculosis* has only rarely given good palliative results, with cessation of abdominal pain and diarrhea.

In *tuberculous adenitis*, probably better and quicker results are obtained in the infiltrative stage with the X-ray. The more enthusiastic advocates of sunlight claim material benefit and cures in over 50 per cent of these cases. Rollier, however, gives a much higher percentage of cures. In suppurating glands it seems better to excise radically, and follow up with solar exposures, although at high altitudes good results are obtained by aspiration followed by sunlight. Hilum tuberculosis in children seems especially suitable for light treatment.

Rollier's results in surgical tuberculosis cannot be denied, but we must remember that the patients remain under his care for prolonged periods and orthopedic principles are in great part carried out.

The part the *air bath* plays in these cases should also be given due credit.

From a consideration of the results obtained with *artificial light* exposures, it appears that in *surgical cases* this means of radiation does not promise as much as sunlight, except in the handling of superficial tuberculosis, enteritis and possibly laryngitis. However, it may act as a fair substitute for sunlight in glandular, osseous, and peritoneal tuberculosis. Longer periods of radiation are necessary.

In *intestinal tuberculosis* exposures to the mercury arc have given palliative results, with cessation of abdominal pain, diarrhea, fever, and bacilli in the stools. The difficulty of judging the clinical results as against controls must be realized. However, this appears to be a real indication for a trial of the lamp. It is hoped that the question of a direct effect upon a focus, such as in the intestine, may be settled by animal experimentation: the disease has been produced in dogs by intravascular inoculation (Loeper and Esmonet).

The use of reflected ultraviolet rays in *laryngeal tuberculosis* is still in the experimental stage.

In order to judge fairly the value of lamps, an institute like that of Jesionek is preferable, where the patients reside permanently and are able to walk about or lie down as they please and do not tire too quickly of the treatment: in this way, they are willing to give it a thorough and conscientious trial.

In *pulmonary cases*, *artificial light* may act as a stimulator of metabolism and a psychic aid; or it may act by depleting, and then in turn causing an overfilling of the pulmonary circulation, this being the result of the cutaneous irritation which brings about a dilatation of the superficial vessels. In pulmonary disease the quartz mercury arc is less dangerous than sunlight and may help individual cases, but we have at present no satisfactory criteria for the selection of these. Any pulmonary case may be given a trial, if only for the psychic effect, The results in some of these cases can prove favorable in the relief of symptoms. In general, brunettes fare better than blondes. *The quartz light seems therefore only an occasional aid for these cases and its advantages should not be exaggerated.* An objection against offering this treatment and one which at present at least seems difficult to overcome is the expense of these lamps. The X-ray may eventually offer a more important method of treatment by directly attacking the lung focus.

Sunlight in pulmonary cases, if employed at all, must be used very cautiously, with a careful selection of the patients, preferably the stationary types, well nourished, who have little or no fever. These are the more favorable cases anyhow. Before attempting the use of sunlight one must realize the dangers that have been shown by experienced workers. Brilliant results cannot be promised. The air bath probably plays a more important part in improving the vigor than has been realized. It must yet be proved whether the light treatment itself specifically helps these cases or whether other factors are not to be given greater credit.

The action of light on ferments and so called "antibodies" and other constituents of the blood, as well as its means of influencing the deeper organs, is mostly a matter of speculation up to the present. Its effect upon protoplasm is not well understood.

The more important ultraviolet rays that especially affect cells, toxins, bacteria, ferments, etc., are present in the quartz mercury lights but absent in sunlight as it reaches us. These are the rays of very short wave length.

We must remember not to become too enthusiastic because of isolated successes nor should we rashly condemn the treatment because of our personal failures.

The exposures should be accommodated to the patient at hand. No general rule can be followed for all cases. Intervals between exposures should be employed in some cases although this may preferably not be the procedure in easily pigmented patients. Cutaneous irritation without tanning can also prove very desirable. The treatment should preferably be given under the guidance of a physician.

Artificial sources of light containing all the rays of the solar spectrum, such as the carbon arc light or the mercury arc combined with incandescent bulbs, may eventually prove preferable, but further experience must determine this. Additional ultrared rays may prove helpful.

Photodynamics has not yet proved a fruitful field therapeutically.

Most of the favorable clinical reports of light radiation still rest upon *empirical evidence.* Scientific work has not yet offered us any very helpful therapeutic results. However, it does seem that light should prove an important means of treatment.

Finally, we must not fail to remember that our personal impressions must be taken for no more than such, and it should be our aim to depend more upon exact experimental data.

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HELIOTHERAPY IN SURGICAL TUBERCULOSIS

REPORT OF RESULTS AFTER SIX AND ONE-HALF YEARS' USE AT THE J. N. ADAM MEMORIAL HOSPITAL

CLARENCE L. HYDE AND HORACE LO GRASSO

Perrysburg, New York

In discussing a paper read by Dr. John H. Pryor before the annual meeting of the Medical Society of the State of New York at Buffalo, April 27, 1915, we predicted that it would not be many years before heliotherapy would be the recognized treatment in the so called surgical tuberculosis. This prophecy is fast being fulfilled, for sun cure is being more generally applied not only in surgical tuberculosis, but also in all conditions where low resistance plays an important part. Several institutions have already made provision for the erection of special buildings for carrying out the Rollier treatment.

In presenting this paper, we wish to bring out the point that during our six and a half years' experience with this method of treatment, we have become so convinced that much better results can be attained in these cases if the disease is not looked upon by orthopedists and surgeons as a purely surgical one. We cannot make it too strong that this type of disease is nothing more than a general constitutional disease with local manifestations, and that it must be treated as such until surgical interference becomes imperative. When we realize that a very large percentage of these cases in adults present also a lung lesion, that comparatively few of them have had a stethoscope placed on their chests, and that it is rarely deemed necessary to call a tuberculosis expert into consultation, it will be readily seen how this disease has been kept a purely surgical one. Until recently not one of our cases of this nature had had a diagnosis of pulmonary tuberculosis made before admission; yet we have had several that have even had positive sputum.

Although sun treatment has been applied for surgical tuberculosis for some years in the United States, it has been practised only in a sort of haphazard way, and consequently the results have not warranted its general adoption. In 1913, Dr. John H. Pryor, after returning from a trip to Europe, was so enthusiastic with the results obtained with Rollier's method of heliotherapy, that he at once introduced it at the J. N. Adam Memorial Hospital at Perrysburg.

In starting the work we encountered many difficulties. Both the medical profession and the laity were very sceptical. We had no proper porches for carrying on the treatment; we ourselves had no special training in orthopedics and surgery; all our nurses and attendants had to be very carefully instructed and closely watched; appliances for immobilization had to be devised; proper wind protection had to be improvised; and, although we were under Dr. Pryor's constant supervision and were following Rollier very closely, we had to modify Rollier's methods to meet our local conditions.

In 1914, on account of the favorable results obtained, Dr. Pryor induced the city of Buffalo to appropriate $125,000 for the erection of two children's sun cure pavilions to accommodate 120 patients. He met with considerable opposition in securing the appropriation because a canvass of all the hospitals in Buffalo showed apparently less than 20 cases of surgical tuberculosis. Within a year not only were these pavilions filled, but we had a long waiting list. Likewise, the pressure for admission from adults was so great that we had to improvise temporary quarters for this class of patients. In 1918, the adult sun cure waiting list became very large, and a temporary building to accommodate 50 men was erected. Today we have under Rollier's treatment 175 cases of surgical tuberculosis as well as many pulmonary ones; and, when our new sun cure pavilions (for which our Council has appropriated $800,000) shall have been completed, our capacity will be more than doubled.

In giving heliotherapy certain precautions must be exercised, and we strongly urge that the directions which we give below be closely followed. Sun cure, when improperly applied, may prove not only unsatisfactory, but very injurious.

After a patient is admitted to the hospital and all casts have been removed, he is made to accustom himself thoroughly to life in the open air before insolation is attempted. This may take a week or more, depending upon the condition of the patient and the weather. The course usually followed is first to have the patient rest and sleep in his room with doors or windows open. Having become somewhat accustomed to the air, he is placed on an open porch for an hour or so. The time is gradually increased until he is able to be in the open practically the twenty-four hours of the day. During this time, he, of course, is either dressed or has full bed coverings, and is not placed under the direct rays of the sun. While he is thus adjusting himself to an open air life, he is carefully observed, and a record is made of temperature, pulse and respiration, and of the urine and blood findings. It is then that he is ready for the real solar bath.

No sun is given later than one-half hour before, or earlier than one hour, or better still, two hours, after a meal. The treatment is carried out in a recumbent position in bed, or, for ambulant patients, on a flat couch, or, if necessary, on the floor. The feet are exposed first without regard to the site of the lesion. The lesions are not to be exposed to the sun until the whole body has been gradually uncovered. Care must be taken that no breeze strikes the body. This can be accomplished by the use of wind breaks or screens. The head is always protected either by a linen cap, umbrella, or awning at the head of the bed. The eyes are shielded by means of colored glasses. We have found that a towel placed over the eyes and forehead proves very satisfactory.

The following schedule is used in giving the sun bath (see chart 1):

First Day. The feet are exposed and bathed in the sun's rays for five minutes, three or four times at hourly intervals.

Second Day. The feet are insolated ten minutes and the legs from ankle to knee five minutes, three or four times at hourly intervals.

Third Day. The feet are insolated fifteen minutes, the legs from ankle to knee ten minutes and the thighs five minutes, three or four times at hourly intervals.

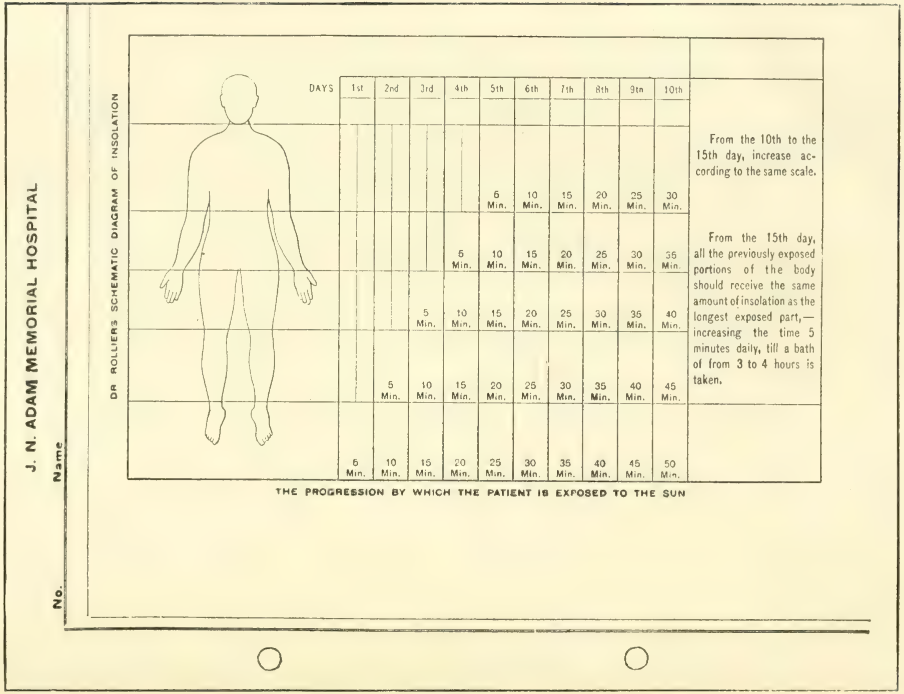
Fourth Day. The insolation of the previously exposed parts is increased by five minutes, and the abdomen and lumbar region are exposed five minutes, three or four times at hourly intervals.

Fifth Day. Again the insolation of the previously exposed parts is increased by five minutes, and the chest and back are exposed five minutes, three or four times at hourly intervals.

Sixth Day. Increase the exposure by five minutes.

The time of exposure is increased daily according to this ratio, until two or three hours of sun bath is given. If the patient's condition does not allow this schedule to be carried out, we insolate the front of the body first, and on the sixth day, or as soon as he can be turned conveniently, expose the back in accordance with the above schedule.

Sinuses and ulcers are not exposed till after the whole body has been insolated, after which the lesions may be covered with a wire screen, so that the sun and air may be allowed to play upon them. It is unnecessary to mention that the only covering that we use after complete insola-



J. N. ADAM MEMORIAL HOSPITAL

Name

No.

DR ROLLIERS SCHEMATIC DIAGRAM OF INSOLATION

DAYS	1st	2nd	3rd	4th	5th	6th	7th	8th	9tn	10th	
					6 Min.	10 Min.	15 Min.	20 Min.	25 Min.	30 Min.	From the 10th to the 15th day, increase according to the same scale.
				6 Min.	10 Min.	15 Min.	20 Min.	26 Min.	30 Min.	35 Min.	From the 15th day, all the previously exposed portions of the body should receive the same amount of insolation as the longest exposed part,—increasing the time 5 minutes daily, till a bath of from 3 to 4 hours is taken.
			5 Min.	10 Min.	15 Min.	20 Min.	25 Min.	30 Min.	35 Min.	40 Min.	
		5 Min.	10 Min.	15 Min.	20 Min.	25 Min.	30 Min.	35 Min.	40 Min.	45 Min.	
	6 Min.	10 Min.	15 Min.	20 Min.	25 Min.	30 Min.	35 Min.	40 Min.	45 Min.	50 Min.	

THE PROGRESSION BY WHICH THE PATIENT IS EXPOSED TO THE SUN

CHART 1

tion of the body is a loin cloth and, as mentioned above, a wire screen. If, however, the discharge is very profuse, we use frequent light gauze dressings to catch the discharge.

After each insolation the patient may be vigorously rubbed with spirits of camphor to harden the skin. If the skin is very sensitive, a rubbing with some vegetable oil, such as cocoanut or olive oil, may be given before each exposure. If, during this preliminary treatment, for any reason the sun bath is interrupted, the insolation should be resumed at a stage a little earlier than that at which it was stopped.

Great care must be taken while the patient is becoming accustomed to the sun, and during the formation of the first pigment. It is at this time that we must be especially careful to see that no reaction such as dermatitis, high pulse, rise of temperature, nausea, headache, or other constitutional disturbances, take place. We must also see that the patient does not overexpose himself, through being overanxious to get as much sun as possible. When there is a great deal of fever, or when the patient is feeble, the time of exposure must be shorter and most carefully regulated. If any reaction is observed, the exposure is stopped or the time shortened.

Throughout the summer months, sun baths are not given during the hottest hours of the day, as a reaction may occur, due to the depressing and fatiguing effect of the sun's rays at this time of the year.

During the winter months, regardless of sun conditions, if a child feels or looks chilly, it is most important that he be taken into a warm room and the treatment discontinued for the time being.

In warm weather the children wear only their trunks, regardless of where they are, whether at play or at meals. On pleasant winter days when the wind is not too strong, the children who can stand exercise play naked in the open for an hour at a time.

After the treatment has been taken for some time, and weather conditions are unfavorable for exposure, an air bath may be given, the length of time depending upon the general condition and resisting power of the patient.

As treatment proceeds, the surface of the skin becomes bronze, then copper color, and finally a chocolate brown. By the time pigmentation has reached this stage, the skin has assumed a soft velvety feel and a healthy look. Its resistance to bacterial infection is now most noticeable. There has not been a case of skin infection after an abrasion in any of our patients, although, during the summer months, the children climb trees and roam through the woods naked, and have every chance of getting abrasions and cuts.

The favorable progress of the cure is in direct proportion to the intensity of the pigmentation of the skin. We use the degree of pigmentation as an index to prognosis. Many of the patients on entering look haggard, anaemic and emaciated, and are fever ridden. Some of them are suffering so much from pain that they cannot stand even the slightest jar. After a very short period of treatment, the general condition of the patient improves remarkably. The fever and chills gradually disappear, and usually at the end of ten days the patient is entirely relieved of pain. We find moreover a return of appetite, and increase in weight and strength, and a better blood condition. Hemoglobin and red cells increase; leucocytosis, if present, becomes reduced; as pigmentation advances, an actual lymphocytosis takes place; eosinophilia is also present to a slight degree; and the patient begins to look like a healthy, happy normal human being once more.

The most striking local result in the treatment of joint tuberculosis by heliotherapy, and the one of greatest importance and advantage in early cases, is the preservation of motion in the affected joint. While Rollier has accomplished this even in cases of fibrous ankylosis where the condition has existed for years, we, as yet, have not been so successful; but we have obtained good motion in early joint cases.

While prognosis, in the ordinary expectant treatment of fixation by casts or by operative procedures, depends upon the completeness of ankylosis, in heliotherapy the gradual establishment of motion goes hand in hand with the healing process. In the classical treatment, ankylosis and the destruction of function are the aims; in heliotherapy, the return of the joint to full function is the aim.

The sun acts as an agent of repair upon bone tissue. There is a separation and a painless spontaneous expulsion of sequestra and an intense recalcification. The point of origin of these sequestra may be quite remote from the point of expulsion. They may follow a sinus tract for some distance.

The effect upon sinuses and ulcers is one of marked reaction on the tract or ulcer. At first there is a profuse discharge, followed by sloughing, formation of healthy granulation and, finally, the drying up and healing of the sinus or ulcer. In cases of abscesses, the sun usually reduces the amount of pus and frequently causes complete absorption. We use no injections of paste nor do we operate. Where drainage is absolutely required, aspiration is resorted to rather than evacuation by incision.

The effect upon lymph nodes is a gradual reduction of their size, and in broken down nodes their contents are often absorbed.

The effect on effusions in joints, peritoneum and pleural cavity is one of absorption. This is most noticeable in peritonitis.

In bone and joint cases a special bed with surgical spring is provided, so that the patient's posture can be properly controlled for counter-traction. The surgical spring is made of strong interlacing steel bands, and may be raised at the head or feet, and to whatever height desired. The use of a hard mattress prevents any possible yielding. Following Rollier's advice, splints are used only in exceptional cases and casts are entirely discarded.

Immobilization is accomplished by absolute rest in bed and by mechanical means, such as chest retaining corsets and tractions, the latter consisting of leather braces connected with straps, the braces gripping the knee and ankle. In this way the pull is at both knee and ankle, and may be increased or decreased at either place as desired. This allows insolation of a considerable part of the extremity.

Time will not permit us to describe the method of treatment for each separate lesion, but such description may be found in an article written by us and printed in the *New York Medical Journal* for January 6, 1917, entitled *The Rollier Treatment for Tuberculosis.*

We have used the Alpine sun lamp for the last five years during the winter months when there was no sun available. Although the results with the lamp are good, it cannot take the place of solar radiation.

For indolent ulcers and sinuses we have used during the past six months with good results the Thézac-Porsmeur lens (a large biconvex lens for concentrating the sun's rays). This lens was presented to us by Mrs. G. T. Post of Newport, R. I. Inasmuch as we have used it for so short a time and in a few cases only, we shall not report results until after further observation.

STATISTICS

In compiling our statistics, we have adopted the following temporary classification for our results of treatment:

Tuberculosis of bones and joints

Apparently recovered. Cases in which all symptoms such as pain, fever, etc., have disappeared, and all sinuses and ulcers have healed. The patient must have been up walking about with no return of symptoms or signs for at least six months.

Arrested. Cases in which all symptoms such as pain, fever, etc., have disappeared, and all sinuses and ulcers show no activity or have healed. The patient may be up and walking about, or may still be in bed.

Improved. Cases in which all symptoms and signs show evidence of improvement.

Peritonitis

Apparently recovered. Cases in which all symptoms such as pain, fever, etc., have disappeared, and all fluid in the peritoneal cavity has been absorbed and palpable masses in abdomen have been reduced. All sinuses and fistulas must be healed. The patient must be up and walking about at least three months without evidence of return of symptoms or signs.

Arrested. Cases in which all symptoms such as pain, fever, etc., have disappeared, and all fluid has been absorbed. Sinuses and fistulas must either be healed or show no signs of activity.

Improved. Cases in which all symptoms and signs show evidence of improvement.

Cervical adenitis

Apparently recovered. Cases in which all symptoms such as fever, etc., have disappeared, and all abscesses and ulcers have healed. The lymph glands must be unpalpable or reduced to nodelike enlargements. This condition is to have existed without any return of symptoms or signs for at least three months.

Arrested. Cases in which all symptoms have disappeared, and all abscesses and ulcers show no evidence of activity or have healed, and the glands have been reduced, but not necessarily to nodelike enlargements.

Improved. Cases in which all symptoms and signs show evidence of improvement.

Tuberculosis of the kidneys

Apparently recovered. Cases in which all symptoms such as fever, pain, etc., have disappeared and the periods of urination have become normal or their frequency has diminished. The urine findings must be negative both by microscopic examination and by animal inoculation. Cystoscopic examination must show healed lesions, if tuberculous cystitis was present. This condition must have existed for at least six months.

Arrested. Cases in which all symptoms such as fever, etc., have disappeared, and frequent and painful urination has abated. Urine findings may be positive or negative.

Improved. Cases in which all symptoms and signs show evidence of improvement.

Tuberculous epididymitis

Apparently recovered. Cases in which all symptoms such as pain, fever, etc., have disappeared, and all enlargement and hardening of epididymis and spermatic cord have been reduced, and sinuses and ulcers have healed. This condition must have existed for at least three months.

Arrested. Cases in which all symptoms have disappeared, and all sinuses and ulcers show no activity or are healed. The enlargement and hardening of the epididymis and spermatic cord must be diminished.

Improved. Cases in which all symptoms and signs show evidence of improvement.

Up to January 1, 1920, 508 cases of surgical tuberculosis were discharged from our hospital. Four hundred and twenty-seven of these remained three months or longer; 13 of them were found to be nontuberculous, thus leaving 414 to be considered in showing the results of treatment.

About 50 per cent of the 414 presented, upon entrance, sinuses or abscesses and secondary infection. Most of them had been operated upon several times because of repeated recurrences of the disease.

Of these, about 60 per cent showed multiple lesions, and a large proportion of the adults showed definite pulmonary signs.

The average length of stay for all the surgical cases that remained longer than 3 months in the hospital was 12.25 months. The length of residence in the hospital has a very definite bearing upon the results of treatment; and the majority of the cases in this report who were dis-

TABLE 1

Results of Treatment of Surgical Tuberculosis from 1913 to Jan 1st 1920 in all cases who remained in the Hospital over 3 months.

Average length of stay 12.25 months

	Glands	Peritonitis	Spine	Hip	Knee	Ankle & Foot	Shoulder	Elbow	Wrist & Hand	Kidney	Epididymis & Testicle	Eye	Osteomyelitis	Sternum	Sacro-Iliac	Lupus	Total
Apparently Recovered	156 or 78%	34 or 79%	10 or 29.4%	23 or 63.9%	7 or 38.9%	7 or 63.6%		3 or 50%	8 or 80%	2 or 14.3%	5 or 62.5%	11 or 91.6%	6 or 50%	2 or 66.7%			274 or 66.1%
Arrested	22 or 11%	6 or 14.9%	8 or 23.5%	7 or 19.4%	5 or 27.8%	2 or 18.1%	3 or 100%	3 or 50%	2 or 20%	7 or 50%	2 or 25%	1 or 8.4%	5 or 41.6%	1 or 33.3%	2 or 100%		76 or 18.3%
Improved	17 or 8.5%		5 or 14.7%	4 or 11.1%	3 or 16.7%	2 or 18.1%				3 or 21.4%	1 or 12.5%		1 or 8.4%			1 or 50%	36 or 8.6%
Unimproved	4 or 2%	3 or 7%	9 or 26.5%	2 or 5.6%	2 or 11.1%					2 or 14.3%						1 or 50%	24 or 5.8%
Dead	1 or 5%		2 or 5.9%		1 or 5.5%												4 or .9%
Total	200	43	34	36	18	11	3	6	10	14	8	12	12	3	2	2	414 or 100%

charged other than apparently cured or arrested left, not because they were not improving, but because they or their families became too impatient.

Although the time required for a cure by heliotherapy is long, nevertheless the results are generally permanent. So far as we have been able to ascertain, there have been but four recurrences of the disease in cases that we have discharged as apparently recovered or arrested. Three were joint cases and one a gland case. The recurrence in the three joint cases followed injury.

Our best and quickest results have been in the closed cases without abscess. When abscess has been present, it has greatly prolonged the treatment, and in those with sinus and secondary infection the progress has been still more retarded.

REMARKS UPON THE TABLE OF RESULTS

Adenitis. The improved and unimproved cases remained at the hospital less than six months, a time really not sufficient to secure results. The case reported as dead died of causes other than tuberculosis.

Peritonitis. Of the cases reported unimproved, one had advanced pulmonary tuberculosis with amyloid changes, had been operated upon before admission, and had an extensive fecal fistula; two had general miliary tuberculosis.

Too much cannot be said for the use of heliotherapy in tuberculous peritonitis. The general improvement of the patient from week to week is most noticeable. Operated cases with recurrence of the disease and unoperated cases respond readily to the treatment.

Spine. One of the improved, although all symptoms and signs had disappeared, did not remain long enough to classify as recovered or arrested, but is now perfectly well and has remained so for two years.

Of the unimproved three remained in the hospital only a short time. One was a very old case of more than twenty years standing, had multiple lesions and had been operated on many times. The rest were progressive cases with multiple lesions and extensive lung involvement, and in four amyloid changes were present.

The two cases that died were doing very nicely before they contracted influenza during the 1918 epidemic, which caused their death.

A large proportion of our cases of Pott's disease had psoas abscesses and had had long periods of treatment in other hospitals before admission to the J. N. Adam Memorial Hospital. All of them showed signs of pulmonary tuberculosis.

Hip. Of the cases reported, 21 or 58.3 per cent had other tuberculous lesions, such as kidney, lungs, glands, peritoneum, etc.; 17 or 47.2 per cent had pulmonary tuberculosis, two of which had a positive sputum; and 18 or 50 per cent had abscesses with secondary infection and profusely draining sinuses. We obtained good motion in 12 or 40 per cent of the recovered or arrested cases, and a partial motion in 8 or 26.7 per cent, making a total of 67 per cent of cases of hip joint tuberculosis, discharged as apparently recovered or arrested, which had serviceable motion.

Knee. Of the 18 cases of tuberculosis of the knee, 12 had lesions other than in the knee; and 9 had pulmonary tuberculosis, two of which had a positive sputum. Of those who were discharged as apparently cured or arrested 10 or 83 per cent had serviceable motion.

Ankle. All of these cases showed other lesions than those of the ankle or foot. Eight or 72.7 per cent had sinuses or secondary infection and had been operated on before admission to the hospital; 5 had a pulmonary lesion. All but one of those discharged as apparently recovered or arrested had full or partial motion. This one had the ankle fixed from a previous operation.

The two cases discharged as improved remained with us only a short time.

Shoulder. Two or 67 per cent of these cases had sinuses and secondary infection. All showed pulmonary tuberculosis; two had a positive sputum.

Elbow. Of the 6 cases of tuberculosis of the elbow, 3 were closed and 3 open. Five or 83.3 per cent had other lesions than the elbow, and 3 or 50 per cent had pulmonary tuberculosis with positive sputum. Those with open lesions and secondary infection had great destruction of the joint and were all fixed. Two of them with closed lesions were well fixed before admission, and there was no more motion upon their discharge. In one there was full motion.

Wrist and Hand. The 10 cases of tuberculosis of the wrist and hand had sinuses and secondary infection. Two had pulmonary tuberculosis. All were completely healed and had good motion.

Kidney. Four of these had one kidney removed with resultant profusely discharging sinuses.

Eleven on discharge showed absence of tubercle bacilli in urine, a diminution of pus and blood and relief of pain, and cystitis. Three still showed the presence of tubercle bacilli, but all other symptoms had improved. All but one, a child, had pulmonary tuberculosis.

Eye. Three of these were complicated with pulmonary tuberculosis, and 4 with tuberculous adenitis.

Osteomyelitis. The lesions in these were localized as follows: 1 in the humerus, ulna and radius; 3 in the tibia; 1 in the femur; 1 in the ilium; 4 in the jaw; and 2 in the ribs.

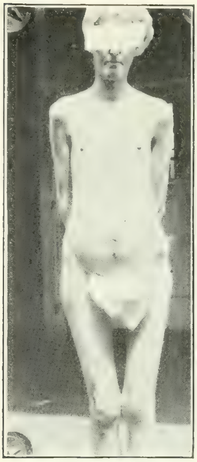
All had sinuses and secondary infection. Many had multiple lesions. Seven had pulmonary tuberculosis, 2 of which had a positive sputum.

Sternum. Both had pulmonary tuberculosis.

Sacroiliac Joint. Both had pulmonary tuberculosis.

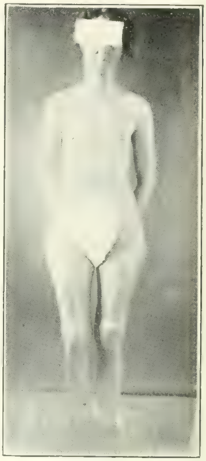
Lupus. Neither of these cases responded to our satisfaction.

The question has been brought up several times as to whether we should not get less deformity than we do. As has been previously mentioned, a large percentage of our bone and joint cases were open cases of long standing, with multiple lesions and secondary infection, and had been operated upon several times. They were cases that had been under treatment for years and had taxed the skill of the orthopedists and surgeons. If we could not correct the deformity, we at least got healing or improvement of the lesions, something that seemed impossible of accomplishing at home where the condition was becoming worse instead of better. We have had but 6.7 per cent of these unfavorable cases that did not respond to treatment, which is a very small percentage. We must not think that heliotherapy will restore joints or motion where there is none, nor that it will cure all cases, but it will certainly do more for so called surgical tuberculosis than any other treatment.

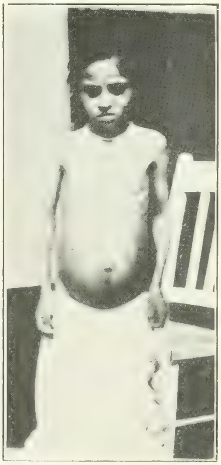


On admission
May, 1919

TUBERCULOUS PERITONITIS
CASE NO. 2412

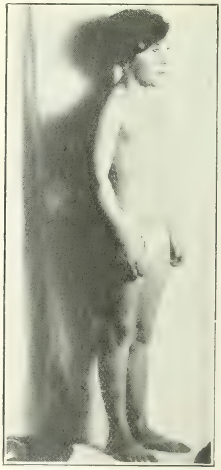


On discharge
April, 1920



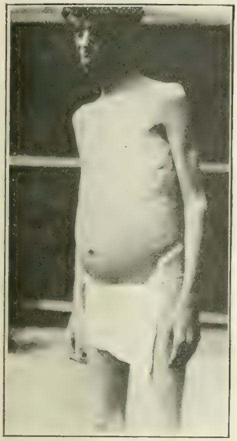
On admission
June, 1915

TUBERCULOUS PERITONITIS
CASE NO. 841

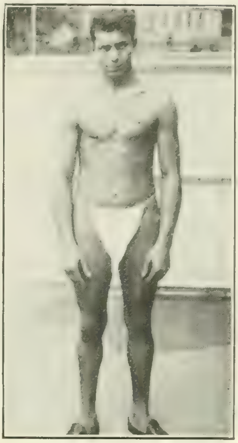


On discharge
November, 1916

Tuberculous Peritonitis
Case No. 1978

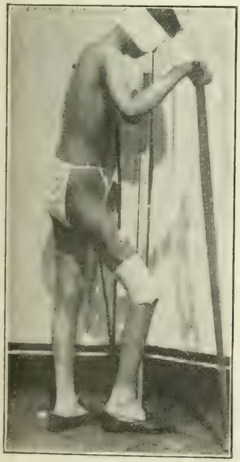


On admission
April, 1918

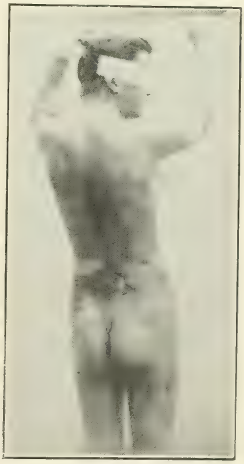


On discharge
August, 1919

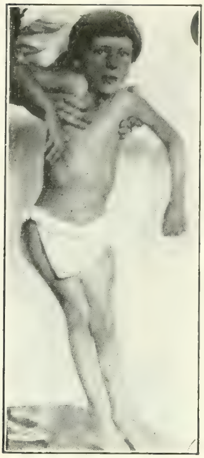
Tuberculosis of Right Hip
Case No. 902



On admission
August, 1915

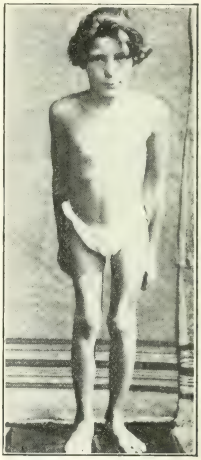


On discharge
January, 1917

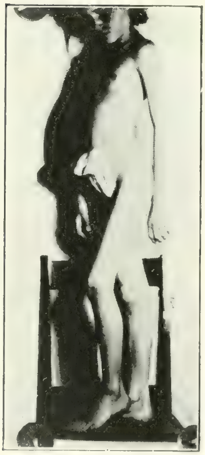


On admission
May, 1915

Tuberculosis of Both Hips
Case No. 832

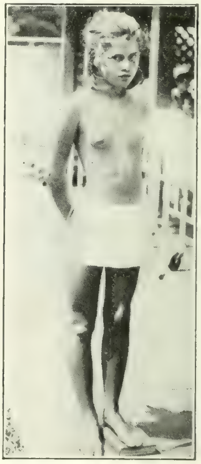


On discharge
April, 1920

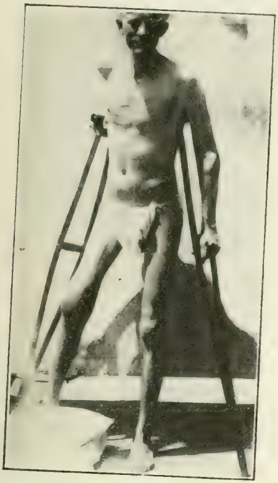


On admission
January, 1917

Tuberculosis of Hip
Case No. 2295

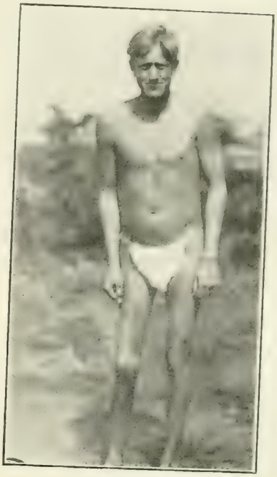


On discharge
August, 1919

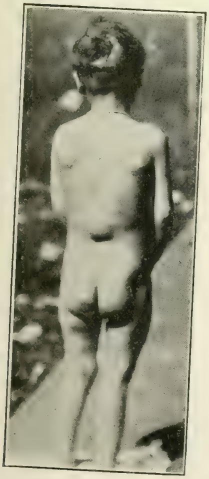


On admission
June, 1916

TUBERCULOSIS OF
RIGHT KNEE
CASE NO. 1283

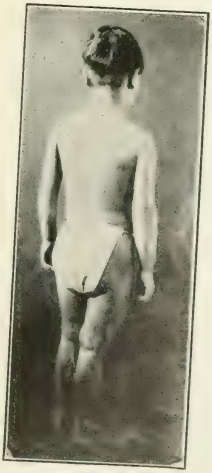


On discharge
November, 1918

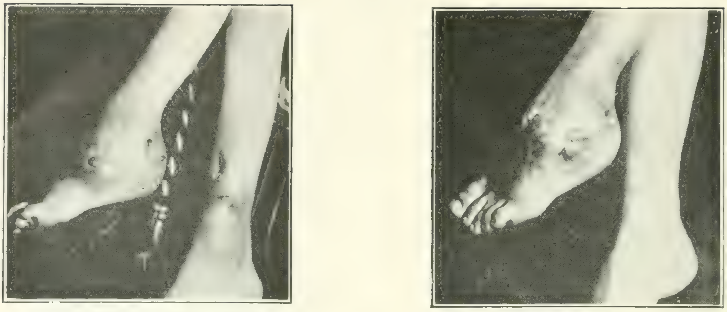


On admission
March, 1919

TUBERCULOSIS OF SPINE
CASE NO. 2319



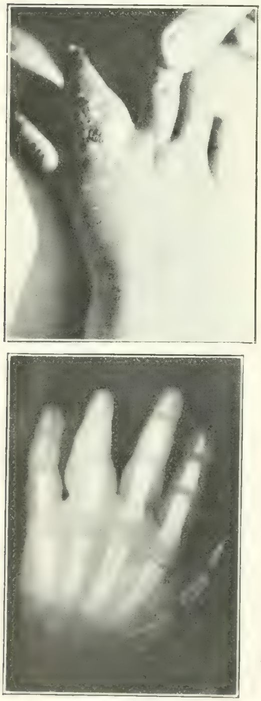
One year later



On admission, January, 1917

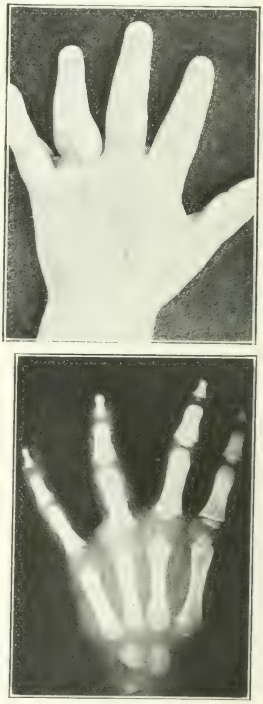
In March, 1920

Case No. 1846. Tuberculosis of Foot and Ankle

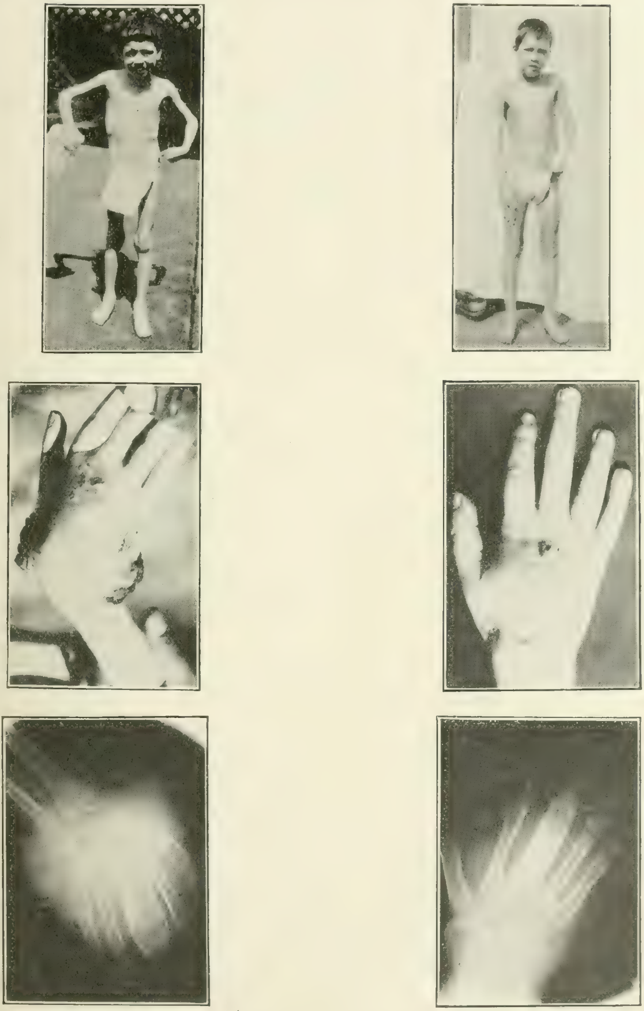


On admission
June, 1918

Tuberculous Dactylitis
Case No. 2078



On discharge
December, 1919



On admission, May, 1919 Ten months later

Case No. 2414. Tuberculosis of Wrist and Hand

THE COSTS OF TUBERCULOSIS[1]

LOUIS I. DUBLIN AND JESSAMINE WHITNEY

New York

This paper is the result of studies made by the Metropolitan Life Insurance Company and the National Tuberculosis Association in order to shed additional light on the question of the economic cost of tuberculosis. Such investigation is a necessary part of the national antituberculosis campaign. Public health work, as now practised, is often expensive. In the effort to obtain the necessary appropriations with which to carry on their work, health officers are learning to utilize figures showing the economic loss sustained by preventable sickness and premature death in their respective communities. Facts of this kind carry much weight with hardheaded municipal authorities. Altogether, the program of health work is by this means put on a much safer footing. Such figures indicate the relative value of the several types of life conservation work when there is competition between them for public attention. Furthermore, they make it possible to show the character of the returns on the investment when work has been carried on for some time. The health officer who approaches his work from the point of view of the economic factors involved is more likely to keep his feet on the ground and to give a better accounting of his activities.

The first step in our method has consisted in preparing a series of life tables. These show, on the one hand, the life expectation including all deaths and, on the other, the expectation with tuberculosis excluded. The differences between the life expectation shown in these pairs of tables thus indicate the average number of years of life lost to each individual in a community because of the presence of tuberculosis; and conversely, the average number of years that would be added to the life span if we lived in an ideal community in which deaths from tuberculosis did not occur, and if other causes of death continued at prevailing rates. The method is not a new one. Professor Glover at the International

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[1] This paper has also appeared in *Quarterly Publications of the American Statistical Association*, December, 1920, to which are referred all readers who may be interested in a statement and description of the mathematical methods involved.

Congress on Tuberculosis held in Washington in 1908 made such a presentation (1), but based it on the male population of the registration states for the year 1900. Our purpose has been to extend these observations to a later date and to include for comparison a group of insured persons among whom a fairly intensive campaign against tuberculosis had been made. Our material is accordingly based upon the experience of the millions of insured wage earners in the Industrial Department of the Metropolitan Life Insurance Company for a period of six years, 1911–1916, and upon the facts for the total population of the registration states as constituted in 1910. This area comprised 21 states and a little over half the population of the entire country. In the insurance experience it was possible to make distinction between the color and sex of the policyholders. In the general population this could not be done and it was necessary, therefore, to limit the study to the population as a whole without finer distinction. The two sets of findings serve as supplements to each other and, as we shall see, confirm in the main the accuracy of the methods employed and of the results obtained.

Table 1 shows for each fifth year of age, beginning with age 0 for the group of wage earners and with age 20 for the general population, the average after-lifetime, both when tuberculosis is present and when it has been completely eliminated as a cause of death.

The loss of expectation of life due to tuberculosis is the difference between the corresponding figures in table 1 at each age and is shown in table 2.

The importance of the disease is indicated by the extent to which it shortens the average span of human life. Among insured wage earners tuberculosis is a very powerful antilongevity force. White males lose 3.5 years in all, or 7.6 per cent of their entire expectancy; white females, 2.6 years or 5 per cent of their expectancy. The heaviest losses occur among the colored people. Colored males and females lose an average of about 5 years of life because of the inroads of this disease, or 12.0 and 13.2 per cent, respectively. On the whole, males lose more heavily than females from tuberculosis. The slightly greater loss among colored females at age 0 is due to the high tuberculosis death rates prevalent among them under age 5; later in life the colored males show much greater losses than do colored females.

There is a gradual decrease with advancing age in the number of years of life lost on account of tuberculosis. Thus at age 20, when productive life is well started for most people, tuberculosis reduces the expectancy 3.7 years among white males, 2.3 years among white females, 4.4 years among colored males, and 3.7 years among colored females. At age 40, the years lost are from one-third to one-half as many as at age 20, and at age 60 and thereafter the losses cease to have an important effect upon longevity although the death rates from tuberculosis continue to be high, even at these advanced ages.

TABLE 1

Average after-lifetime of specified populations, with and without tuberculosis—all forms. By color and by sex for insured wage earners, 1911–1916, and for total population of registration states, 1910

AGE	METROPOLITAN LIFE INSURANCE COMPANY, INDUSTRIAL POLICYHOLDERS, 1911–1916								POPULATION, REGISTRATION STATES, 1910	
	White				Colored					
	Males		Females		Males		Females			
	Tuberculosis present	Tuberculosis absent	Tuberculosis present	Tuberculosis absent	Tuberculosis present	Tuberculosis absent	Tuberculosis present	Tuberculosis absent	Tuberculosis present	Tuberculosis absent
0	46.0	49.5	51.8	54.4	37.2	42.2	38.6	43.7	*	*
5	50.3	54.1	55.2	58.0	45.0	50.6	46.1	51.6	*	*
10	46.1	50.0	51.1	53.8	41.1	46.5	42.4	47.7	*	*
15	41.7	45.5	46.7	49.3	37.1	42.2	38.6	43.3	*	*
20	37.4	41.1	42.5	44.8	33.8	38.2	35.7	39.4	44.2	46.6
25	33.5	36.8	38.5	40.4	30.8	34.4	32.9	35.5	40.3	42.3
30	29.8	32.6	34.7	36.1	27.7	30.6	29.8	31.7	36.5	38.1
35	26.4	28.6	31.0	32.0	24.9	27.1	26.7	28.0	32.7	33.9
40	23.2	24.9	27.3	28.0	21.9	23.6	23.6	24.5	28.9	29.9
45	20.1	21.3	23.5	24.0	19.1	20.3	20.6	21.2	25.2	26.0
50	17.2	18.0	19.9	20.3	16.4	17.2	17.7	18.1	21.6	22.1
55	14.4	14.9	16.4	16.7	13.8	14.4	14.9	15.2	18.1	18.5
60	11.7	12.0	13.3	13.5	11.4	11.8	12.3	12.5	14.9	15.2
65	9.3	9.5	10.6	10.7	9.5	9.7	10.1	10.2	11.9	12.1
70	7.3	7.4	8.4	8.5	7.7	7.9	8.0	8.1	9.4	9.5
75	5.7	5.8	6.7	6.7	6.4	6.5	6.3	6.4	7.1	7.2
80	4.6	4.6	5.1	5.1	5.4	5.5	5.3	5.3	5.3	5.4
85	3.6	3.6	4.0	4.0	4.5	4.5	4.5	4.5	4.0	4.0
90	2.9	2.9	3.0	3.0	4.0	4.0	4.1	4.1	2.9	2.9
95	2.4	2.4	2.4	2.4	3.1	3.1	3.2	3.2	1.9	1.9

* Data not computed.

The loss in years of life is obviously greater among insured wage earners than among the general population because tuberculosis death rates are uniformly higher among the industrial groups. But even in the general population the loss in years is 2.4 at age 20, 1 at age 40, and 0.3 of a year at age 60.

The extent of the damage from tuberculosis appears to be closely associated with the life expectancy of the population in question whether we consider tuberculosis as a factor in mortality or entirely eliminate it. The loss from tuberculosis is high where longevity is low and is low where longevity is high (see table 3). Thus at age 0, tuberculosis decreases the span of life 3.5 years for insured white males, but only 2.6 years among the longer lived white females, and about 5 years among the much shorter lived colored policyholders. The coefficient of correlation between longevity and the loss of longevity due to tuberculosis, based upon one hundred observations among insured wage earners, is 0.791±0.076.

TABLE 2

Loss in years of average after-lifetime due to tuberculosis—all forms

AGE	METROPOLITAN LIFE INSURANCE COMPANY, INDUSTRIAL POLICYHOLDERS, 1911–1916				POPULATION, REGISTRATION STATES, 1910
	White		Colored		
	Males	Females	Males	Females	
0	3.5	2.6	5.0	5.1	*
5	3.8	2.8	5.6	5.5	*
10	3.9	2.7	5.4	5.3	*
15	3.8	2.6	5.1	4.7	*
20	3.7	2.3	4.4	3.7	2.4
25	3.3	1.9	3.6	2.6	2.0
30	2.8	1.4	2.9	1.9	1.6
35	2.2	1.0	2.2	1.3	1.2
40	1.7	0.7	1.7	0.9	1.0
45	1.2	0.5	1.2	0.6	0.8
50	0.8	0.4	0.8	0.4	0.5
55	0.5	0.3	0.6	0.3	0.4
60	0.3	0.2	0.4	0.2	0.3
65	0.2	0.1	0.2	0.1	0.2
70	0.1	0.1	0.2	0.1	0.1
75	0.1		0.1	0.1	0.1
80			0.1		0.1

* Data not computed.

This suggests that the conditions of constitution and environment which determine the mortality from tuberculosis also in a measure determine the death rates from other important causes. Another possibility which must be considered is that the amount of mortality from tuberculosis may be determined by the prevalence of certain diseases which like typhoid fever, malaria, hookworm, and syphilis, undermine resistance; and that, conversely, tuberculosis, when prevalent, helps to impair physical vigor and thus increases the death rate from the so called "degenerative diseases," such as heart disease, Bright's disease, and arteriosclerosis. All three factors are probably at work in different degrees in different communities. Tuberculosis does not stand isolated but is closely bound up with environmental conditions on the one end and constitutional factors on the other, being determined by and determining the rate of loss from other diseases. This question is being attacked by means of a study of the losses of longevity from other important causes and will be reported upon at a later date.

TABLE 3

Table for 100 observations among insured wage earners, 1911–1916, of the Metropolitan Life Insurance Company, showing correlation between longevity and loss in longevity from tuberculosis*

		Longevity		Totals
		Low	High	
Loss in Longevity	High	a 43.5	b 7	a+b 50.5
	Low	c 15.5	d 34	c+d 49.5
	Totals	a+c 59	b+d 41	N 100

* The 100 observations consisted of 25 random ages for the series White Male, White Female, Colored Male, and Colored Female. The dividing lines between high and low for any series were furnished by the average longevity and the average loss in longevity from tuberculosis respectively, for that particular series.

Our next step was to express the losses in expectation described above in terms of estimated money losses. The importance of tuberculosis as a factor in national economy is in this way brought home more sharply. After an examination of the available data on wealth, income, and production in the United States, we concluded that a loss of one year of life was equivalent to a money loss of not less than $100 in national wealth. This conclusion was submitted to a group of economists who have busied themselves with such questions and they confirmed this estimate as in accordance with the best data available. We may say, therefore, that each year of life expectancy lost from tuberculosis by the population of the United States represents a loss of $100 in national wealth. In view of the fact that tuberculosis mortality cuts approximately two and one-half years from the complete life expectation of every individual under present mortality conditions, the loss per person is at least $250. This, in a population of approximately one hundred and six millions, represents a loss of twenty-six and a half billions of dollars. The present generation would add that much more net wealth if tuberculosis were not a factor in mortality. Since the average lifetime is approximately fifty years in the United States, this loss means an annual charge in excess of five hundred million dollars from the curtailed longevity of individuals because of tuberculosis.

No consideration has as yet been given to the very large additional losses which result from the long periods of sickness due to tuberculosis. The losses from disability for work, the cost of medical, nursing, and extra dietary and other care, add very materially to the figures quoted above. It is not possible for us at this time to offer even an estimate of this loss. The amount is enormous. One of us in a study of the records of the Association for Improving the Condition of the Poor (New York City), which has for a number of years conducted intensive relief measures for the care of tuberculous families, found that a tuberculous family was under care, on the average, for a period of two years, four and one-half months, and that during this time the families suffered a wage loss of $836 and the Association contributed $1,181 in relief and care. These data are not sufficient in themselves to determine the community loss in tuberculous families, but they suggest how much the items will be when more extensive and more detailed information becomes available.

Our study has shown the important part that tuberculosis plays as a factor in modern economic life. The amount of damage done is great enough to justify large expenditures for the control of tuberculosis as a cause of sickness and death. The tuberculosis death rate has declined and is still declining. Among industrial policyholders of the Metropolitan Life Insurance Company the death rate has in recent years been reduced very rapidly. In this organization special efforts have been made to instruct the great body of policyholders in methods of preventing and combating the disease, apparently with good results. The death rate from tuberculosis of the lungs in the entire experience has declined 30.3 per cent between 1911 and 1919. During 1920, to date, the experience is reaching low figures previously thought to be unattainable. In fact, the tuberculosis death rate of insured wage earners is now almost as low as in the general population, although ten years ago there was an excess of 41 per cent in the death rate among these people as compared with that of the general population. In view of the complexity of the problem it is not possible to measure with any exactness the direct relation between the various efforts expended and the results obtained by the antituberculosis campaign. Yet the results are indicative that the work has borne fruit. These achievements clearly call for a continuance of the antituberculosis program along the lines now being followed.

REFERENCE

(1) Glover, J. W.: Monetary loss in the United States due to tuberculosis. Proceedings Sixth International Congress on Tuberculosis, 1908, p. 55.

THE REASON AND REMEDY FOR MISSING THE EARLY TUBERCULOUS LESION

HENRY F. STOLL

Hartford, Connecticut

While it is probably true that pulmonary tuberculosis is as a rule diagnosed earlier than a few years ago, the cases that are unrecognized till the disease is well advanced are still very numerous. Is it not strange that the disease, concerning whose symptomatology and physical signs so much has been written, should still prove a stumbling-block to so many. We know that occasionally the disease advances so slowly, almost hand in hand with immunity, that the amount of involvement is considerable before any symptoms are manifest. Such cases were occasionally picked up by the tuberculosis boards in the army; they are however uncommon.

We frequently hear it said and with some truth that the patient is to blame for not seeking medical advice till long after symptoms became manifest. In a small group of cases studied several years ago, I found that the average delay in consulting a physician after the development of symptoms was nearly six months. But in many instances a meagre history is taken and no examination made at the first consultation. In fact, it is not uncommon to meet with patients who consulted several physicians before being examined. There is, however, another reason for missing the early cases, more important, I believe, that those already mentioned. During the world war, as instructor in the diagnosis of tuberculosis at the Medical Officers' Training Camp at Fort Benjamin Harrison and later at the Army Medical School in Washington, I had the opportunity of observing the ability of the average physician in general practice to diagnose early tuberculosis. My impressions are based upon an intensive course of instruction given to about three hundred physicians, who coming as they did from all parts of the country can be considered as fairly representative of the profession at large. I am speaking now of the man with average ability who has not made a special study of tuberculosis. My first impression was that he is very apt to miss the early lesion, not as a rule through any lack of honest endeavor on his part but because he does not know what signs to look for, or how best to elicit them. He is apt to believe that dulness is present with tuberculosis, but how to percuss and how to evaluate dulness if detected, he is quite at a loss. The valuable information furnished by inspection is rarely sought for and the procedures used to elicit râles and their differentiation from various adventitious sounds are quite unknown. One is forced to conclude that the instruction in this subject given in the medical schools has hitherto been inadequate. Several times it seemed that even recent graduates of class A schools were quite unfamiliar with the signs of the normal chest and unless the normal be mastered how can the pathological be recognized? Secondly, I was impressed with the enthusiasm with which they set about the work. The doctor in general practice has little time to make a special study of any particular branch of medicine; accordingly the various postgraduate courses in the army were very popular. Thirdly, I was a good deal surprised to see that a considerable degree of diagnostic skill could frequently be acquired in so short a time. I recall two men especially. One had done only surgery for about fifteen years and acknowledged that he knew nothing about tuberculosis; the other was an obstetrician. Yet fate decreed that they should help free our army from tuberculosis. Both developed a high degree of skill not only in the detection of physical signs but in their proper interpretation.

If then it be true that the basic reason for the failure to recognize tuberculosis is the lack of knowledge as to how to elicit physical signs, what is the remedy? If this information could be disseminated by medical journals or text books each and every doctor would be an expert, so numerous have been the articles on early diagnosis during late years. Postgraduate courses are essential. The three thousand men who received the instruction in the army will do more to further the early diagnosis of tuberculosis than anything that has hitherto been done. In fact, Colonel George E. Bushnell's idea of teaching physical diagnosis was one of the big medical ideas of the war. For several years an excellent course in the diagnosis and treatment of tuberculosis has been given at the Trudeau School of Tuberculosis at Saranac Lake. The United States Public Health Service has recently been giving intensive courses in the diagnosis of tuberculosis in a number of the Western and Southern States. The course which lasts seven days has so far been only available to physicians attached to the Public Health Service but they hope shortly to give the courses for all who may wish to attend.

Similar courses could be given at some of the large state institutions throughout the country and would undoubtedly prove popular as was demonstrated this past summer in Maine. Following a suggestion made a year ago, by Dr. Edward O. Otis, a short intensive course was given at the Central Maine Sanatorium in Fairfield and sixty-six physicians registered, a large number for the first year. Practically all expressed a desire to return the following year. Of course, no one would for a moment imply that one week's intensive instruction in any medical or surgical subject would make a thoroughly qualified specialist;—the fine points in differential diagnosis can only be acquired by years of experience. But it is possible in a short time to show how to correctly examine the lungs, to touch upon some of the more important points in differential diagnosis and to impress the need of repeated sputum examinations. Most important of all perhaps is the awakening of an interest in the subject and the stimulus given for further study.

As an aid to what might be termed the orthodox methods of instruction mention should be made of the use of motion pictures. During the late war when it was necessary to teach wholly inexperienced men highly technical subjects in a short space of time, the motion picture was invaluable. Standard methods of instruction were carefully worked out and filmed and by the use of animated drawings, the workings of intricate machinery were at once understood by the merest tyro. We have all laughed at Mutt and Jeff at the movies but not many know that during the war several of the best known of the animated cartoonists were busily engaged in Washington making animated drawings for the Surgeon General, illustrating various medical and surgical subjects.

In order to make the course in the diagnosis of tuberculosis available to those not in the service, an attempt was made to put it upon the screen. Since we were absolutely unfamiliar with everything pertaining to motion pictures and actively engaged in hospital work at the time this was undertaken, there is much to criticize in the finished product. Yet, imperfect as it is, from the criticism it has received I feel that it has demonstrated that this means of instruction is of some value in the teaching of physical diagnosis and we may look forward to the not too distant future when much better pictures will be produced dealing with a great variety of medical and surgical subjects.

It seems that the overcrowding of the curriculum of the medical schools might be lessened if motion pictures were used as an aid to other forms of instruction. It was found at West Point, for instance, that by the use of animated drawings a certain course could be fully covered in fifteen minutes that previously required twenty-four lectures of one hour each. Another advantage of this method of teaching is the fact that one will sit for a considerable time and look at a picture dealing with a subject that he would not spend five minutes in reading about. Obviously the greatest advantage is that it takes the clinic to the doctor who is too busy to go to the clinic.

CONCLUSIONS

1. The chief reason for the failure to recognize early tuberculosis is not so much ignorance as to what the signs are, as the lack of knowledge of how to elicit them.

2. The establishment of short, intensive courses of instruction in diagnosis at the state tuberculosis sanatoria throughout the country is much to be desired.

3. The motion picture appears to be of some value in teaching physical diagnosis.

STUDIES ON TUBERCULOUS INFECTION

VIII. SPONTANEOUS PNEUMOKONIOSIS IN THE GUINEA PIG

HENRY STUART WILLIS

From the Kenneth Dows Tuberculosis Research Fund, of the Medical Clinic of the Johns Hopkins Hospital and University

INTRODUCTION

It is now almost five years since this series of studies on tuberculous infection was planned. Originally projected to elucidate, eventually, well known phenomena of localization and progression of human tubercle, it proceeded from basic results of experimental infection which had long been recognized.

In the rabbit, for instance, infection always tends to pile up in the lungs; in the guinea pig, however, the lungs accumulate relatively little lesion until late in the course of infection or unless very large numbers of bacilli are applied directly to the lung (by inhalation or intravenous inoculation). On the other hand, the spleen of the guinea pig seems peculiarly "susceptible;" that of the rabbit relatively escapes infection. In the guinea pig with little *intrapulmonary* tubercle, infection of the tracheobronchial nodes which drain the lung is prominent (study VI by Krause) while the rabbit with massive infection in the lungs is prone to show but little in these nodes.

Thus far in the studies it has been found that, as between the lung of the guinea pig and that of the rabbit, the normal structure varies in so fundamental a way as to be decisive in determining differences of haemotogenous distribution to this organ in the two animals (study IV by Miller and study V by Willis). And data thus far accumulated suggest the generalization that the origin and development of tuberculous infection in the guinea pig are peculiarly influenced by the lymphatic anatomy of the several organs of its body (study VI).

An important part of the plan of these studies must be to attempt to influence and change what might be called the normal or natural localization of infection by altering the lymphatic system of animals of experiment. Doctor Willis has undertaken this investigation, using various inorganic dusts as his experimental media. But before presenting the results of this work, and by way of laying the foundation for it, he has exhaustively investigated the pulmonary localization of inert foreign particles in guinea pigs which have naturally and without experimental interference acquired spontaneous anthracosis by reason of long confinement indoors. The advantages of such a study are plain and it is to be hoped that it may throw light upon some features of experimental anthracosis which have remained obscure because of technical obstacles.

Allen K. Krause.

The studies of Mall on the liver and intestine and those of Miller on the lung are prominent among anatomical productions which have reëmphasized the importance of the relation between normal structure and pathological lesion. Recent studies on tuberculous infection from the Kenneth Dows Tuberculosis Research Fund (1) have shown directly the intimate relationship existing between the normal lymphatic system of the lung and tuberculous infection of that organ in the guinea pig. It has been pointed out that, once the invading microörganism passes the respiratory mucosa or the vascular endothelium, it is brought into the domain of the lymphatics. There is great probability that the first tissue to be involved in tuberculous reaction (anatomical) of the lungs is the lymphoid tissue[1] and it may be ventured that the dependence upon the lymphoid system of initial pulmonary tuberculous processes is established. It becomes obvious then that conditions influencing the lymphatic system of the lung will likewise influence to a greater or less extent the degree and course of tuberculous infection involving these tissues.

In an effort to understand more exactly what is the rôle of the lymphatic system in tuberculous infection of the lung, we have undertaken to modify the normal structure and physiology of the pulmonary lymph apparatûs by subjecting experimental animals to the inhalation of dust. The effort has been carried out with two purposes in mind, namely, (1) to determine the effect of prolonged dust inhalation on lung tissue, especially the effect on the lymphatic system; and (2), having rendered the lung abnormal by the inhalations, to ascertain the influence of its altered anatomy upon infection with the tubercle bacillus.

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[1] This refers to the lymphoid tissue as sites of focalization, and not to lymphatic cells as such.

Dust was the medium chosen for three reasons: first, because *a priori* there is reason to believe that with dust the lymphatics might fairly easily be "plugged;" secondly, because the lymphatic tissue, under the irritant influence of dust, undergoes proliferation and thus probably sets up changes (resistance to flow) in lymph physiology; and thirdly, because it has long been maintained that among workers in certain dusts the morbidity and mortality rate from tuberculosis is excessively high.

Before the experiment had passed the preliminary stages, a wide variance in results appeared. By this time, too, the writer had found numerous discrepancies reported in the literature, and Doctor Krause suggested that a knowledge of what happens to dust breathed by normal animals *under natural conditions* might greatly facilitate an interpretation of the moderate or advanced pathological picture produced under the conditions of experiment. Attention was consequently directed to the condition of the lungs of fifteen normal guinea pigs all of which had been confined indoors for two years or more; and the work to be presented first, therefore, is a report of a study of spontaneously acquired dust in the lungs of normal, caged guinea pigs. That dust accumulates spontaneously in the lungs of guinea pigs which have lived long in confinement must have been observed by many workers who have had occasion to keep animals for fairly long periods; for, after a cage life of a year or longer, the lungs of guinea pigs always show gross discoloration. The treatment of the experimental data to be presented on pneumokoniosis and tuberculosis will appear later.

No consideration of the findings in spontaneously dusted lungs can be properly taken up until we have discussed in some detail the whole subject of dust and the lung.

Since the middle of the eighteenth century when autopsies were first performed with any sort of regularity, discoloration has been observed in the lungs of certain human individuals, particularly in those of adults who were city dwellers. Pearson (2), in 1813, stated that he had extracted a black powder from the bronchial nodes and from the lungs, and that he had established its identity in every case with that of charcoal. He observed that the pigment was laid down in an orderly manner and believed, from a comparison of his specimens with Cruikshank's drawings of the pulmonary lymphatics (3), that the charcoal was laid down along the lymphatic vessels. He remarked, "as hath been repeatedly observed, the lungs generally become more dark coloured proportionately to their age;" and he advanced the idea that dust reaches the lungs with the inspired air and is transported *by lymphatics* from the air spaces to the bronchial nodes.

The idea was prevalent at the time that Pearson wrote and later, that lung discoloration represented different maladies which fell into three main groups and were classified as (1) healthy black matter, (2) true melanosis and (3) spurious melanosis. But Craig (4) declared in 1834 that the inhalation of dust was responsible for all the forms of lung black and that the different stages of "melanosis" represented merely varying amounts of charcoal in the lung. Thomas Graham (5) wrote also in 1834 and, accepting Pearson's work, suggested that miners' lungs were black because the miners had inhaled carbon from their oil lamps, and explained the lack of symptoms in these cases on a basis of the smallness and therefore nonirritating properties of the carbon particles. The term *anthracosis* was suggested in 1838 by Stratton (6) to distinguish the condition from the more malignant *melanosis*.

A great deal of experimental work has been done since 1867, when Knauff (7) definitely established (by devising the first dust inhalation experiment) the relationship between lung pigmentation and dust laden air. This worker exposed certain dogs to smoke and others to an air suspension of ultramarine blue for varying periods of time and subsequently recovered particles of the substances from the lungs of the exposed animals. Arnold (8) made what is probably the most complete study of experimental pneumokoniosis yet reported. The study was published in 1885 and is a detailed account of the whole pathology of pneumokoniosis. In the work he exposed dogs and rabbits to various dusts for relatively long periods of time and found accumulations of dust in the alveoli and their septa, in the lymph nodes, in islands of lymph tissue throughout the lung, and in fibrous tissue nodules which develop in the lung in response to the continued presence of irritating dusts. In his report comment was made on the fact that dust in the lymphatics themselves was noted only very infrequently.

The position of Pearson and his followers did not go unchallenged, however, and numerous able pathologists, especially in Germany, stoutly maintained that the inhalation concept did not represent the truth. Early the belief was that the bronchial nodes secreted a bluish black substance which was responsible for their discoloration and, in a way imperfectly understood, responsible also for the discoloration of the lungs. Virchow (9) held in 1847 that lung pigment is derived from haemoglobin. After Traube (10) isolated particles of carbon from a coal miner's black lung (1860), Virchow (11) finally admitted (1866) the possibility of the inhalation of dust and the further possibility that such dust might cause lung discoloration. In the same year Koschlakoff (12) had contended that, because he could find little or no pigment in the alveoli and their walls when it was constantly present in the walls of the larger bronchi, the pigment was formed from within and therefore from the blood.

But even the Virchow admission did not settle the question for all time, for it was again raised in 1905 when Vansteenberghe and Grysez (13) sought to support Calmette's contention. Calmette (14), in studying tuberculous infection, had maintained that the digestive tract is the portal of entry for the tubercle bacillus which produces pulmonary tuberculosis. To show that this circuitous route is the normal one for foreign matter in the lung, Vansteenberghe and Grysez fed various dusts to animals and in this manner claimed to have produced lung pigmentation. They noted the significant fact that the age of the animal (guinea pig) is important in the study of pigmentation of lung tissue. In their experiments they found the lungs of adult animals pigmented and those of young animals free from pigment and concluded that lung pigment enters the body by way of the digestive tract; in young guinea pigs this pigment is prevented from reaching the lungs by the relatively impervious mesenteric nodes, whereas, in old pigs, the foreign matter is not so held up for the reason that the mesenteric nodes become permeable with age. They brought forth this idea as an hypothesis without presenting sufficient evidence to support it. But the work of Oliver (15), written from extensive clinical and laboratory experience, that of Montgomery (16), and that of Findlay (17), each of whom did exhaustive pigment feeding experiments, seem definitely to establish the air route as the prevailing portal of entry for the dust which produces pulmonary pigmentation.

NATURE OF DUSTS

Some dusts are injurious; others can apparently be inhaled for years with impunity. Explanations of this fact fall in general into a consideration of the nature of the "particulate" matter. Organic dusts are comparatively harmless (Landis, Oliver, and others). The following properties of the inorganic dusts are said to determine the degree of harm they may produce:

A. Physical properties:
  1. The "hardness" or "softness" of the particles, and
  2. Their size and shape
B. Chemical properties:
  1. The chemical power of the particles as irritants
  2. Their property of absorbing organic substances
  3. Their solubility, and
  4. Their chemical reaction

With respect to the question of the "hardness" of dusts, Oliver (18) has stated that it is wholly the physical character of the dust that is important. Soft coal dust, he held, is much less harmful than hard coal dust, and that of hard coal much less harmful than that of rock, while dusts from silica or from siliceous material are quite injurious. He cited in this connection the work of Claisse and Joué (19) who exposed animals to smoke from burning turpentine for long periods and produced an extensive though delicate pigmentation of the lung; but the discoloration, even though extensive, was apparently quite harmless to the animals. Mavrogordato (20) compared the effects of the inhalation of coal, shale, "flue" dust, precipitated silica, quartz, and flint dusts, and found the most damaging results to ensue from the harder dusts. Landis (21) remarked that the severity of lung lesions varies "in accordance with the hardness, sharpness, and chemical composition" of the dust and that silicotic dusts may produce "serious damage" to the lungs.

The researches of Watkins-Pitchford and Moir (22) have also thrown much light on the physical character of dusts. Upon studying silicotic lungs (from gold miners of South Africa) they found that by far the largest numbers of particles of foreign matter in pigmented lungs are smaller than one micron in length, that the mean measurement of 100 particles taken consecutively and drawn to scale was 6.13 by 2.18 microns, that no particle was larger than 13 microns, and that *the prevailing form of the particles in such lungs in general is narrow and elongated with one or both ends sharp and pointed.* They felt that phagocytes show a selective action for small and elongated forms. A polariscope was used in their work.

Concerning the irritating properties of dusts, Mavrogordato (20) believed that the dusts which irritate the mucosa promptly upon introduction into the lung are the very dusts which do the least permanent injury. His feeling was that there is an immediate reaction to irritating dusts on the part of the respiratory epithelium, marked by an engulfing of the foreign elements by the epithelial cells, and that this is followed by a desquamation; these shed "dust cells" form a bolus to which, with mucus, other cells, dust particles and debris attach; these "plugs" are then spat up and in this way much of the foreign matter is removed before it ever actually reaches the lung parenchyma. The rate of elimination, he felt, is as important as the rate of intake.

Haldane (23) agreed with Mavrogordato (20) that the baneful influence of dusts in the lung is determined largely by whether the particles are removed from the organ or are retained in it, and, in seeking an explanation of this fact, suggested that it is those dusts which readily absorb other substances (water, tissue juices, etc.) that are most promptly removed from the lungs. Carbon, shale, and other like dusts possess this property to a marked degree; and he advanced the idea that these particles become increasingly attractive for phagocytes as they continue to absorb more substances, whereas, the more crystalline, nonabsorptive particles—flint, quartz, silicon, etc.—are, in their nakedness, less attractive for the dust carrying cells. This idea presupposes that the inert dust particles reach areas where absorption of tissue juices is possible before phagocytes act upon them. On the other hand, many believe that certain dusts, instead of absorbing body fluids, are dissolved by these. In his Milroy Lectures in 1915 Collis (24) called attention to the possible significance of the acidity of dusts (silicon) which "may render the particles capable of entering into and modifying the structure of protoplasm."

AGENCY OF DUST TRANSPORTATION

Particulate matter is breathed in with the inspired air and is found in many parts of the lung parenchyma. By what means is the transportation from air space to tissue effected? The idea has been advanced by some (Sikorsky, Klein[2]) that particles have the capacity of passing directly between uninjured epithelial cells. Traube (10) felt that the angular nature of the particles enables them to pierce the epithelium, and Rindfleisch[3] thought the impact of the inspired air sufficient to drive particles through this structure.

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[2] Quoted from Klotz.

But most workers oppose the view of penetration of the tissues by pigment without the agency of some intermediary carrier and agree that the transportation is effected by cellular (phagocytic) activity. The nature of the phagocyte, however, has been many times questioned. Knauff (7), Wainwright and Nichols (25) and others regarded the *epithelial* cell as a phagocyte, and it was Arnold's (8) belief that the bronchial and alveolar epithelium and "lymphatic wandering cells" are all capable of phagocytic activity. Oliver (15) partially agreed with Arnold; and, according to him, wandering cells of the pulmonary alveoli (originally alveolar epithelium, apparently) may be the dust carriers. (He regarded these large phagocytes as probably normal inhabitants of the alveolar spaces.) And he believed that the cells acquire their loads of dust and leave the alveoli through stomata to gain the lymphatics.[4] Klotz (26) held with Haythorn (27) that pigment may be demonstrated in a variety of cells but that the phagocyte which commonly engulfs dust is an "endothelial leucocyte," is the same cell referred to in pathology as "epithelioid," and is a fixed tissue cell. Still another viewpoint is presented by Mavrogordato (20) who described dust as being within "fixed tissue" cells, by which from the context he apparently meant both reticulum and alveolar epithelium. Watkins-Pitchford (28) spoke of phagocytes as being "catarrhal and leucocytic."

REACTION OF THE LYMPHATICS IN THE DUSTED LUNG

Throughout the literature there is a general though vague agreement that dust is "handled" by the lymphatic system—once it gets out of the air passage; but much confusion has existed as to exactly what part of the lymph system is involved, and what the effects are on that system and on the lung. Certain workers (Klotz, Watkins-Pitchford, Oliver) believed that the first reaction consists in a proliferation of the cells of the fibrous layer of the terminal blood vessels, and, to a lesser extent, of that of the small bronchi. These areas, they held, correspond to the situations of lymph channels, and in their judgment the reaction is in the nature of a perilymphatic induration, in the fibrous tissue of which new increments of foreign matter become incarcerated: the thickening at the same time offers obstruction to the normal lymph flow and ultimately invades surrounding tissue after the fashion of a malignant growth (Watkins-Pitchford). It is only later on in the process, they would say, that a fibrosis occurs in the masses of lymphoid tissue, but when this does happen the masses ultimately become transformed into fibrous (silicotic) nodules.

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[3] Quoted from Klotz.

[4] Miller has shown (*The air spaces in the lung of the cat. J. Morph., 1915, xxiv, 459*) that "stomata" or "pores" are artefacts.

On the other hand, Watt, Irvine, Johnson and Steuart (29), in a report on miners' phthisis in the South African mines, said that the initial reaction is a fine fibrosis in and around clumps of dust cells which are caught up in masses of lymphoid cells along the course of the lymphatics. In this, Landis, Mavrogordato, and others agreed, although Mavrogordato believed that the dust cells are present in the lymph nodes only transiently, that they ultimately reach the bronchial or other nodes near the hilum and from thence work through the fibrous wall of the large bronchi, gain the lumen and are eliminated through expectoration. Johnson (30), who kept white rats in the gold mines of the Witwatersrand for more than two years and killed them off at various intervals, occupied a middle position and reported that the foreign matter is most densely aggregated in the lymph "nodules," but is also always present in the loose connective tissue around the small blood vessels and bronchi, particularly just under the pleura. He noted dust cells frequently in the lymph sinuses of the bronchial and other nodes, and thought a fibrosis to be the essential lesion. This, indeed, is the one point on which all authors agree.

SPONTANEOUS PNEUMOKONIOSIS

The inference from this survey must be that the whole matter is buried in misinterpretation and doubt, and it seems reasonable to expect a study of the anatomical and pathological relations of normally acquired pigment in animals to clarify some points in connection with the findings in clinical and experimental pneumokoniosis.

Causal relation between natural anatomic changes in the lung and the presence of dust has been noted by Miller (31), who called attention to differences in anatomic structures in the human lung at different ages. He found a strikingly small amount of lymphoid tissue in the lung of the infant, more in the child, and a gradual increase with increasing age. Singularly enough, he found pigment in increasing amounts with increasing amounts of lymphoid tissue, and he concluded that the dust particles act as irritants which stimulate the proliferation of such tissue.

In the human lung natural pigmentary deposit develops with age: this is also true in the lung of the caged guinea pig, and the gross discoloration is, in some cases, extreme. Generally, in the oldest pigs, the lungs are beautifully pigmented, particularly so in the middle lobes in the areas which are most pendant when the animal is in its normal posture. The black matter is laid down in wide, irregular lines which connect freely with one another to form, more or less imperfectly, many four, five and six sided figures. It is also laid down in localized spots. Some of these are sharply outlined: others are of poor definition. This foreign matter is also spread throughout the entire organ, the color of which is generally pale gray instead of a normal pink,—"marbled" as Pearson aptly described it. The color in the bronchial nodes varies a good deal, depending upon the amount of their pigment content; and accordingly these structures appear pearly gray, blue, or black. These discolored nodes are enlarged, the black ones greatly so. Figure 1 illustrates the lung of an adult guinea pig with its acquired pigment. The pigment here is more dense in the cephalic and middle lobes, and the entire organ has a pale, grayish tint. The drawing is of natural size and was done in natural color.

1. Anatomic Considerations. There exists much the same intimate relationship between pigment and lymphoid tissue in the lung of the guinea pig as has been shown to exist in human and other mammalian lungs, and it is germane to consider briefly the normal arrangement of this tissue before discussing its content of dust. It has been pointed out repeatedly by Miller (32) and others that lymphoid tissue is distributed in a characteristic fashion in the mammalian lung. With the lung of the guinea pig the situation is of interest because the normal lung of this animal (of the size usually used in experimental work) *contains an uncommonly small amount of lymphoid tissue—an amount often so small as to escape notice in a microscopic examination of the tissue.* In this respect it resembles closely the lung of the infant or the child. Despite its *paucity of lymph tissue,* this lung contains unusually large and numerous lymphatics; and lymph drainage should, therefore, be freeer than in animals where a greater number of lymph masses would tend to obstruct the drainage tubes (lymphatics) or to slow the lymph circulation. It has been termed an "open" lung. In the matter of lymph anatomy this animal stands in great contrast to certain other animals of experiment, notably the rabbit; for the lung of the latter contains relatively much more lymphoid tissue and relatively fewer and smaller lymphatics and is said to be more comparable to the lung of the adult human being. The guinea pig, therefore, lends itself peculiarly to work of the kind here reported, because one can here note lymphoid changes with comparative ease and certainty. Several of the above points and the significance of the pulmonary lymph anatomy and physiology have been reëmphasized and elaborated lately by the work of Krause (33).

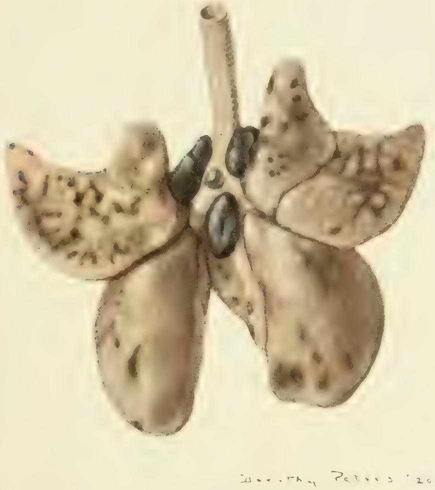

FIG. 1. LUNGS FROM A NORMAL GUINEA PIG WHICH HAD LIVED A CAGE LIFE FOR MORE THAN TWO YEARS

Ths discoloration is more marked in the pendant portions of the middle lobes and in the tracheobronchial nodes which are considerably enlarged. The drawing was done in natural color and is of natural size.

In the lungs of old guinea pigs which have been caged for more than a year several unique features are present: First, there is *an increase in the amount of lymphoid tissue; larger and more numerous masses are seen in the normal situations for such tissue.* In many instances these masses have acquired definite "nodal"[5] characteristics; they are prominent along bronchi and blood vessels and occasionally under the pleura. Figure 2 shows the relative size of a mass of these cells to the small bronchus which it accompanies. Secondly, large deposits of lymph tissue, not normally situated, are also present. Cordons of lymphoid cells[6] are thrown around the pulmonary artery, especially in its smaller branches at and beyond the level of the *bronchiolus respiratorius* and in

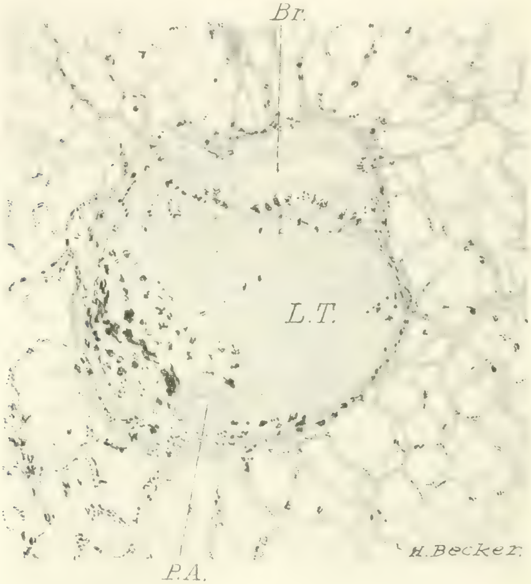

FIG. 2. A LARGE MASS OF LYMPHOID TISSUE REPRESENTED IN ITS RELATION TO THE AIR PASSAGE

Normally there should be but a few cells here. Dust is present especially in the peripheral parts of the mass. *Br.*, bronchus; *PA*, pulmonary artery; *LT*, lymphoid tissue. × 92.

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[5] "Nodal" is used simply to indicate the presence of a spherical mass of lymphoid tissue without germinal centres.

[6] It is probably true that a very few cells are normally present here—so few as to escape ordinary observation in single sections—and that these have proliferated under the stimulus incident to the presence of dust.

particular at dividing points. These masses are irregularly arranged and, although in cross section they sometimes appear as discrete nodules, they are in reality irregularly fusiform, elongated lymphoid masses which encircle the vessel. It is interesting to note in this connection that Irvine and Watt (34) described an irregular periarterial thickening as one of the early lesions in pneumokoniosis and remarked that the thickenings are not "nodular" formations. Some idea of the shape and relative size of these masses may be had by reference to figure 3 which is a photograph of a plaster model reconstructed from camera lucida drawings of serial sections. The mass of tissue shown here surrounds the artery irregularly at one of its points of division. In figure 4 a section through the lymphoid formation illustrated in figure 3 is shown at a point where it surrounds the artery. In the third place, lymph masses not infrequently develop in the lung parenchyma,[7] apparently

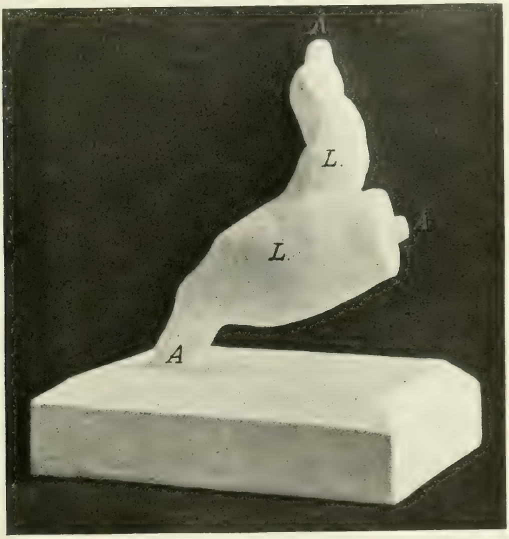

FIG. 3. A PHOTOGRAPH OF A MODEL RECONSTRUCTED FROM SERIAL SECTION DRAWINGS

The irregular mass of lymphoid tissue follows the branches of the artery for some distance both proximal and distal to the point of division. A section from this tissue is shown in figure 4. *A*, pulmonary artery; *L*, lymphoid tissue. × 40 or 45.

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[7] It is possible too, that normally there are a few cells in these situations.

without obvious relation to blood vessel or air tube. These "nodules" appear to have their origin in the tissue *back* of the alveolar epithelium where they may embrace an area as large as three or four alveoli. They are seen most often in the apices and near free lung borders and are illustrated in figure 5 which is a camera drawing of a section from the apex of the lung of a guinea pig more than two years old. Numerous small islands of lymph tissue are scattered through the lung parenchyma, and in some of these considerable dust has collected.

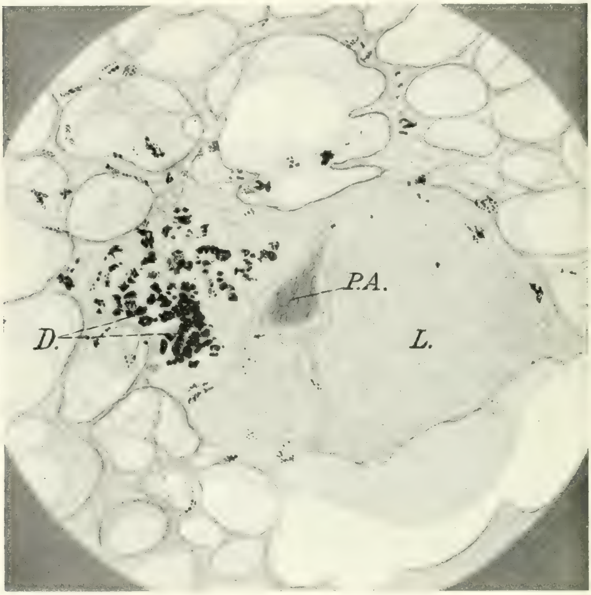

Fig. 4. A Retouched Photograph of a Cross Section Through the Lymphoid Tissue and Pulmonary Artery Shown in Figure 3

The lymph tissue completely surrounds the vessel and contains a considerable number of dust cells. *D*, dust; *P.A*, pulmonary artery; *L*, lymphoid tissue. × 205.

2. *Pigment relationships.* Particles of pigment may be found in practically all tissues of the lung. Most of them are intracellular, or are lying in small masses which have been left upon the death of the phagocytes.

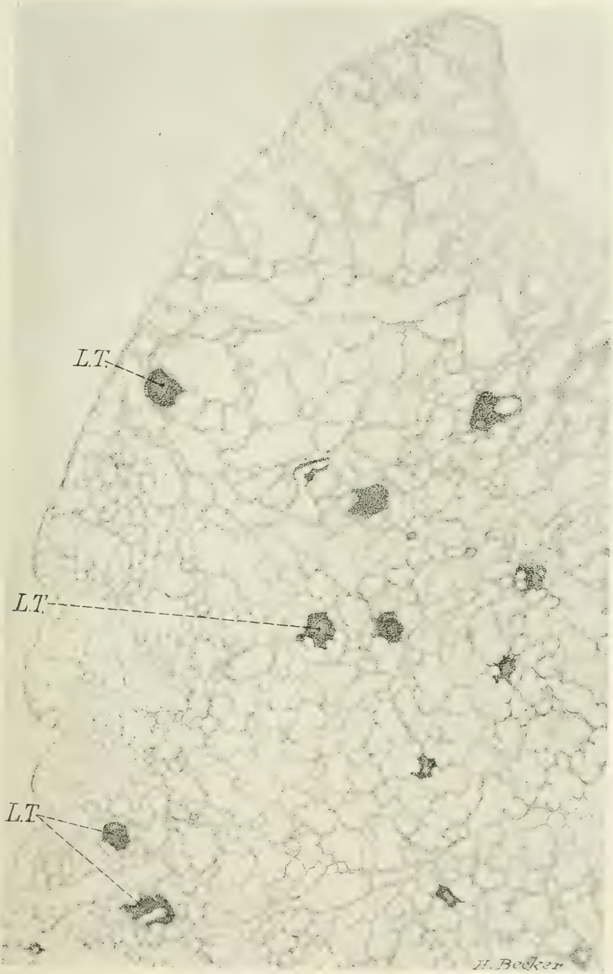

FIG. 5. LOW POWER CAMERA LUCIDA DRAWING OF A TIP OF A LOBE FROM AN OLD GUINEA PIG'S LUNG DRAWN TO ILLUSTRATE THE UNUSUALLY LARGE NUMBER OF LYMPHOID CELL MASSES

Some of these are in association with air passages and blood vessels; others are apparently without obvious relation to these structures. Most of them contain dust cells. *LT*, lymphoid tissue. × 40.

a. Relation to the pleura. The deposits of dust and their relations to the pleura are best studied in specimens cleared in benzene and oil of wintergreen;[8] for the cleared lung, when properly treated by this method, is an object of beauty and shows in its translucency numerous black spots and a network of black lines. Many of the spots are suspended just under the pleura without apparent supporting structure. They develop at and near the points where pleural branches of the pul-

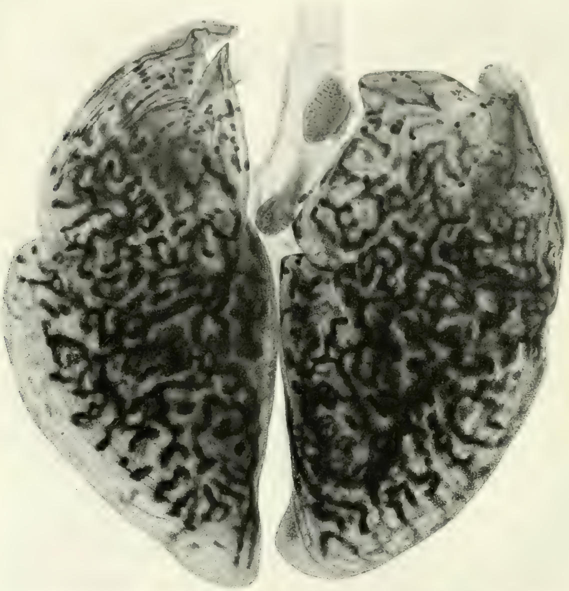

FIG. 6. DRAWING OF A LUNG OF AN OLD GUINEA PIG IN WHICH THE MARKINGS HAVE BEEN INTENSIFIED BY A SHORT PERIOD OF ARTIFICIAL EXPOSURE TO DUST

The lines mark off indistinctly some of the outlines of the secondary lobules. The fine polygonal markings represent the dust deposits in alveolar walls. One of the bronchial nodes has been removed. × 21.

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[8] Spalteholtz method. The tissue is fixed in 10 per cent formalin containing a few drops of glacial acetic acid, dehydrated, passed from a second change of absolute alcohol to benzene and thence, after several hours, to oil of wintergreen.

monary vein begin and they thus have a more or less regular arrangement on the lung surface, corresponding in all probability to the situations of the points of junction of the septa which mark off the secondary lobules in the lungs of certain other mammals. They are starting points for the development of the lines which appear later. The lines often vary; some of them are short, others are long; some lie within or just underneath the pleura while the ends of others dip into the depths of the lung tissue. These markings are illustrated in figure 6 which is a drawing of a lung from an animal more than two years old. The picture here is accentuated by having the animal artificially exposed to dust for a short time.

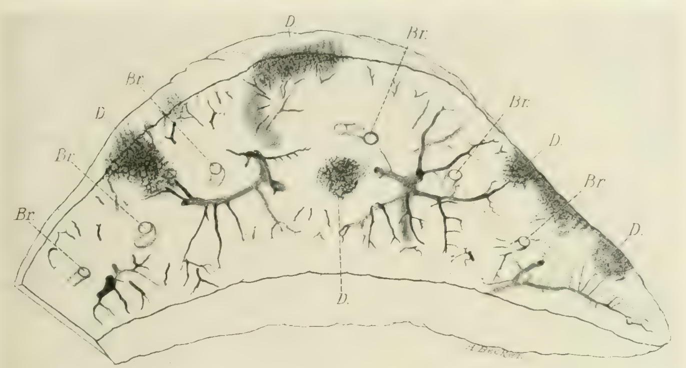

FIG. 7. A RETOUCHED CAMERA DRAWING OF A THICK, FREE HAND SECTION SHOWING BRONCHI, DUST PATCHES, AND VEINS

The dust deposits show a remarkable alternation with the bronchi. In several instances the vein is seen to be arising from the pleura in the collection of dust. *Br*, bronchus; *D*, dust. The heavier lined vessels are veins. The arteries are not shown. Refer to figure 8. For further description see text. × 6.

That the arrangement of the dust in the pleura has a definite basis is evident from both gross and microscopic examination, and the basis apparently rests on the anatomical relations of the parts involved. The spots of dust are situated in the corners of the lobule (secondary lobule of Miller[9]). As has been stated, these points correspond to places where the larger pulmonary vein radicles begin, and thus to the areas representing junction points of the lobular trabeculae in the lungs of man and other mammals possessing a thick pleura. The lines which connect many of the spots correspond to the borders of the secondary lobules which, in certain other lungs, are marked by the trabeculae just mentioned. These relations can best be appreciated by reference to figure 7 in which is illustrated a regular, orderly, alternating relation of dust patch to bronchus. The patches of dust represent sections through spots; the cross cuts through lines. The patches of dust correspond rather regularly to the limits of the lobules to which the alternating bronchi lead and represent in general the relationship further illustrated in figure 12. The bronchus situated between two given areas of dust divides at numerous places and sends many branches in various directions, but the main continuations of the branches pass ultimately toward the spaces which hold the dust. The figure is a camera drawing of a thick (0.5 cm.) free hand section of a cleared lung.

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[9] Strictly speaking there is in the normal guinea pig no definitely demonstrable secondary lobule, for this term relates to the areas marked out by the anatomic dipping down of trabeculae from the pleura of animals in which this tissue (pleura) is thick. But structurally the likeness is striking.

Microscopically, the areas of black lie in large part just underneath the pleura and consist of aggregations of dust carrying cells located in various tissues as follows: Some are grouped in the masses of lymphoid tissue which are frequently present; some are in the alveolar wall behind the epithelial layer; a few lie occasionally within the pleura; others lie in the intact alveolar epithelial cells which appear without doubt to occupy a normal place in the alveolar wall; still others are out in the alveoli themselves, often clumped in small groups. No pigment cells have been observed *within* a *pleural* lymphatic. A retouched photograph of a section through one of the black spots is shown in figure 8. The dust cells are shown here in relation to the different elements of the involved area. The pleura and the alveolar walls are slightly thickened.

b. Relation to lymphoid tissue and lymphatics. There is a good deal of pigment in the masses of lymphoid tissue mentioned above. Pigment laden cells, "caught" in this tissue, particularly in its outer parts, give it the appearance of a slight or moderate "peppering," though they are rarely present in sufficient numbers to give it a solid black color. Occasionally pigment cells lie within these lymphatics but the rule is to find that these cells have wandered through the lymphatic wall, immediately outside of which they *may* be found in considerable numbers; here they may mark the course of a lymph channel as it lies in the wall of an air tube or blood vessel. It is this black deposit which often marks the outline of bronchi and blood vessels seen in gross examination of pneumokoniotic lungs. Arnold, it will be recalled, commented on *the paucity of dust within the lymph channels.*

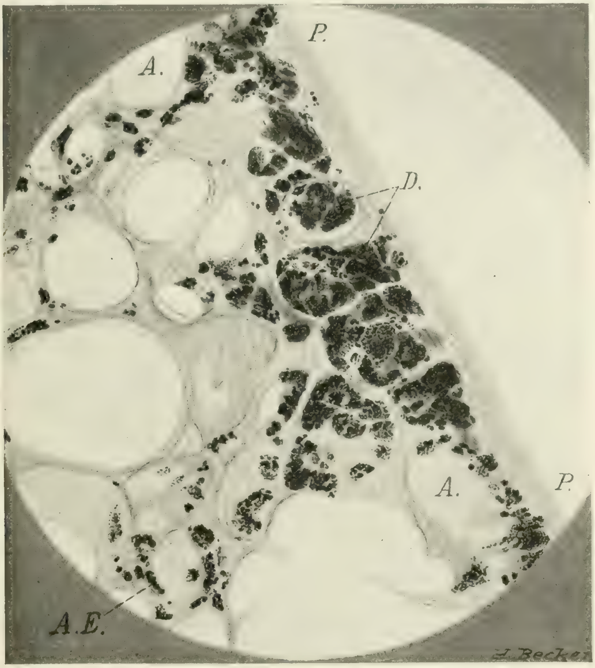

FIG. 8. A RETOUCHED MICROPHOTOGRAPH OF ONE OF THE SPOTS OF DUST IN AND UNDER THE PLEURA

Further description is given in the text. Refer to figure 7. *P*, pleura; *A*, alveolus; *AE*, alveolar epithelial cell containing dust; *D*, dust in alveoli. A few dust particles lie in the pleura. × 205.

c. Relation to the tracheobronchial nodes. The tracheobronchial nodes are not uncommonly *the most densely pigmented tissue in the respiratory apparatus of these old guinea pigs.* They become increasingly black with age and they may range in color from a faint grayish tint to jet black. They hold the dust in a characteristic manner. Some of the dust cells lie scattered through the medullary portion of the nodes;

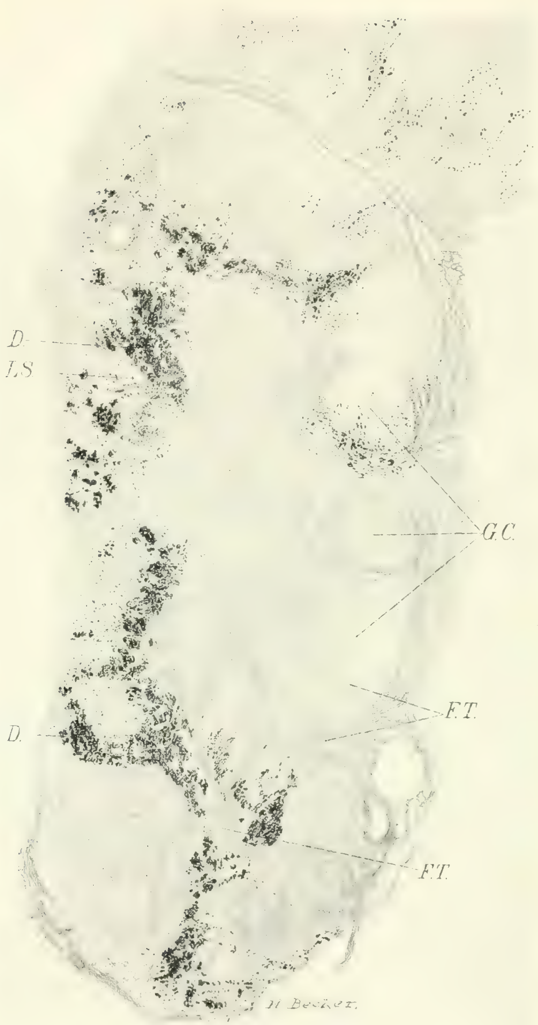

FIG. 9. A SECTION THROUGH A BRONCHIAL NODE IN A GUINEA PIG MORE THAN TWO YEARS OLD

The dust cells tend to be grouped near the lymph sinuses and around and between germinal centres. Some dust is also scattered throughout the node. None is seen within the lymph sinuses. Some fibrosis is evident. *D*, dust around germinal centre and lymph sinus; *FT*, fibrous tissue; *GC*, germinal center; *LS*, lymph sinus. See figures 10 and 11. × 36.

but perhaps the larger number of them lie in groups that are seen both in the immediate periphery of the lymph sinuses (where they are often present in sufficient numbers to attract attention to the situation of these channels) and in regions lying between the germinal centres, especially at points where three or four germinal centres lie near together. This corresponds to the situation in which the first signs of fibrosis develop. The dust content of the tracheobronchial nodes is illustrated in figure 9 which is drawn from a section through a node from a normal guinea pig that was more than two years old. The pigment is densely collected around and between germinal centres and around the lymph sinus, but not within it. This arrangement is further illustrated in figure 10. The node shown here was cleared in benzene and oil of wintergreen and is reproduced in its natural, unstained condition. The little clumps of dust cells lie between groups of germinal centres, and the dark linear markings (see figure 10) probably represent the course of lymphatics or of sinuses.

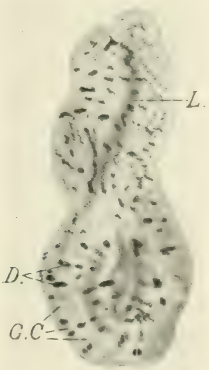

FIG. 10. A TRACHEOBRONCHIAL LYMPH NODE FROM AN OLD GUINEA PIG

The node has been cleared. The spots of dust represent dust collections in areas between germinal centres, especially between situations of three or four of the centres. The dim outlines of dust indicate the course of lymphatics, or lymph sinuses, which are marked out by the dust deposits along their course. *GC*, area of germinal centre; *D*, dust between germinal centres; *L*, outline of lymph sinus or lymphatic. Refer to figures 9 and 11. × 10.

d. Relation to the alveoli. Pigment *cells* lying free in the alveoli of the lungs of old normal guinea pigs is a common finding; free *pigment* in the alveoli is only infrequently seen. How long these cells may remain in the air spaces is a matter of conjecture, but their *absorption* must be relatively slow, since in these normal animals increments of dust are taken into the lung only very slowly and gradually, yet the dust cells are always seen. Haythorn (27) felt that they may lie in the alveoli for several months.

Pigment is frequently seen in the alveolar epithelial cells, especially in the "corner" cells made so much of by Sewell (35) who, by intravenous vital staining methods, showed that the alveolar epithelial cell rather than the vascular endothelial cell is actively phagocytic for dust in the lung. Briscoe (36) and others have made the same claim. On the other hand Permar (37), McJunkin (38), and others have recently adduced good evidence that endothelial cells are the scavengers of lung dust. The cytology of the phagocyte has not been studied in this work and the question must be dismissed with the statement that it *seems*, from histological appearances only, that more than one type of cell is involved in the process. It seems equally true that the alveolar epithelium should be regarded as one of the types. In the loose tissue just behind the epithelial layer there are numerous dust laden cells.

e. Relation to the bronchi, arteries and veins. These relationships have practically been discussed because the *relation of the dust to lymphatics and lymphoid tissue* (paragraph *b* above) refers entirely to the lymphatics and lymphoid tissue lying in the walls of the bronchi, arteries and veins. Within these structures one finds the dust cells that have wandered through the walls of the lymphatics, and have been caught up in the loose areolar in which they course, plus those which have been held in the lymphoid tissue—itself in close relation to the wall of air tube or blood vessel.

3. Fibrosis. The essential end reaction of pulmonary tissue to the presence of foreign matter is a fibrosis. On this all investigators are agreed. In the opinion of many (Watt, Irvine, Johnson and Steuart, Koltz, Watkins-Pitchford, and others), the fibrosis arises in very close relation to the lymphatics and lymphoid tissue. Wainwright and Nichols (25) felt that the thickening occurs first in the alveolar and interlobular septa. According to Johnson (30), the enlargement of the lymph nodes and especially of the tracheobronchial nodes is due to a connective tissue proliferation in the nature of replacement tissue, and, notwithstanding the increase in the size of the node, its content of lymphoid elements is probably lessened. Thus, this worker thought, nodules develop in the lung as a fibrous tissue reaction in and around the original lymph node or original mass of lymphoid cells which as a filter had gathered to itself irritating particles of foreign matter out of the lymph. Most authors have felt that the irritating bodies along the course of the lymph channels and in the masses of lymphoid tissue stimulate the fibrous reaction and that the process is continued, until with certain dusts a relatively large proportion of lung tissue has been encroached upon by the scarring and is destroyed.

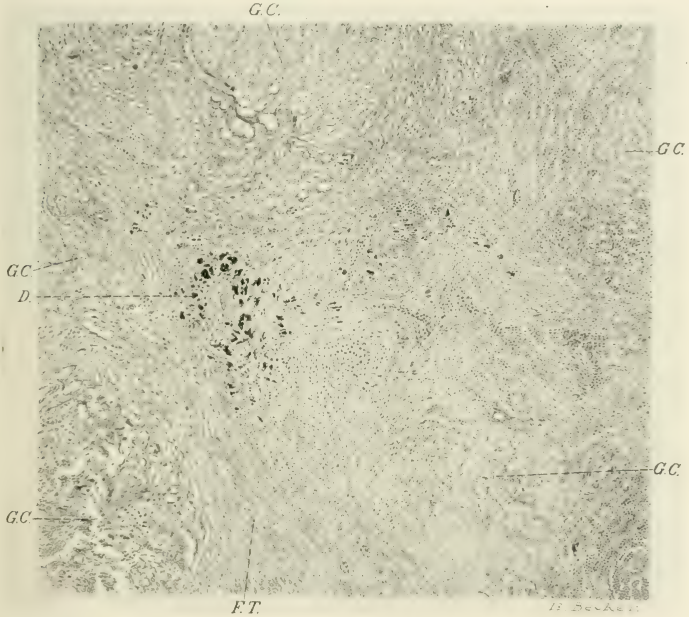

Fig. 11. A Camera Drawing Through a Portion of a Tracheobronchial Lymph Node Showing Dust Particles in the Midst of Fibrous Tissue Which Has Encroached on the Normal Lymphoid Tissue of the Germinal Centres

Some of the dust cells appear to lie in small sinuses. *GC*, germinal centre; *FT*, fibrous tissue; *D*, dust. See figures 9 and 10. × 114.

A minimal amount of fibrous tissue formation is encountered in the lungs of old guinea pigs and is to be seen chiefly in a mild thickening of the pleura and alveolar septa where collections of dust cells are found, and in the tracheobronchial nodes where some of this tissue develops between and around the germinal centres. The new tissue formed in thesereg ions contain dust cells. Figure 11 was drawn to show the fibrous process in a tracheobronchial node.

DISCUSSION

The matter of first importance in a consideration of the findings just reported is the fact that the work was done on *the lungs of normal adult animals* which had lived long enough to have developed lung pigmentation under the natural conditions of cage life. One of the outstanding features in the study of these normal animals is an anatomic one and consists in the presence of a *relatively large amount of lymphoid tissue.* Masses of the tissue may occasionally be seen on the freshly cut surface of the gross lung, lying near the larger bronchi and blood vessels at the hilum. These are very conspicuous in microscopic sections. In general they are definitely nodular and possess germinal centres. They appear in the situations in which such tissue is normally found in many mammalian lungs; namely, at the dividing points of bronchi, bronchioli, and blood vessels, and occasionally at points in the pleura where branches of the pulmonary vein arise. They also appear in situations unusual for such tissue in younger animals—animals of the size and age more generally used in experimental work.

The significance of this tissue has been suggested by Miller (31) who thought it must arise as a reaction to the presence of irritating dusts in the lung, and this explanation seems altogether the probable one. For in the natural course of events a certain minimum of the dust breathed into the lung is carried past the epithelial barrier and into the closed system of pulmonary lymphatics where, in the ebb and flood of the lymph, some of it is caught and held permanently or transiently in the small masses of lymphoid cells intercalcated along the course of the lymphatics. Here this foreign matter stimulates the cells to proliferative activity, and, as they become larger, the chances are increasingly better that these masses may act as more efficient mechanical filters simply by virtue of their size and may thus hold up many more dust cells; these new irritating bodies in turn stimulate the lymph tissue to greater proliferation and the resulting increase in size of the masses continually enhances their obstructive possibilities.

Gardner's recent contribution (39) lends added evidence to this idea of proliferation of the lymphoid tissue under the influence of irritant dusts. This worker exposed guinea pigs to granite dust for as long as seven months, and observed that, for a considerable time, before there was any macroscopic lesion demonstrable, the masses of lymphoid tissue in the lung appeared very active and showed many mitotic figures.

It should be borne in mind, however, that the dust particles stimulate other than the lymphoid elements, for these particles are also responsible for the formation of a small amount of fibrous tissue in the walls of air passages and blood vessels where the lymphatics course, and particularly in the lymph nodes at the hilum.

Ultimately dust reaches the tracheobronchial nodes in considerable quantity and this is what one would expect from the work of Miller (40) and others who have shown that practically *all*[10] lymph in the lung flows toward the hilum and the tracheobronchial nodes. The dust in the alveoli is engulfed by phagocytes and carried through the alveolar walls into the irregular tissue spaces which might possibly be thought of as "unformed lymphatics." From here much of it is carried by the ebb and flow of the lymph to and through the lymphatics and past the lymphatic tissue barriers to the tracheobronchial nodes. On the journey, however, many of the dust cells filter or wander through the thin walls of the lymphatics and are held in the areolar tissue with which these channels are environed; here some degree of fibrosis may also occur. The fact that dust accumulates around the sinuses and lymphatics of the nodes indicates that something of the kind will happen in the lung if the quantity of dust is sufficient. With the continuous addition of dust (or infection), the central depots (nodes) become clogged, and as this occurs, pigment (by blocking) will extend more peripheralward (as will infection also).

The tendency for the dust to become deposited in the areas that limit the secondary lobules at the pleura offers perhaps more basis for conjecture than for clear cut explanation, but it seems probable that two or three anatomical factors may produce these markings. The first of these is the fact that in its branching within the lobule the bronchus sends its main divisions toward the edge of the lobule at the pleura. This is indicated in the accompanying illustration—figure 12, which is a camera drawing. The more direct air current with its dust is obviously along the larger and more direct branches of the air passage. Small dust deposits occur under the pleura at the terminals of these two direct passages. A second factor which may contribute toward the laying down of the dust in these areas is the fact that in the areas of the black spots and junction points of the lines there is often a small mass of lymphoid tissue which would tend to hold the dust. Although it is quite difficult to demonstrate lymphatics in the zone of the black lines, one feels that they must undoubtedly be present and that their presence as dust carriers might account for the dust collections along the avenues of travel.

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[10] *All* with the possible exception of that in the vessels of the diaphragmatic pleura. See *Cunningham, R. S.: Contributions to Embryology, Carnegie Institute of Washington, 1916, iv, no. 12, Publ. no. 224.*

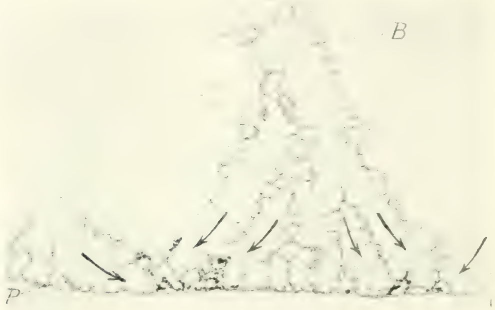

Fig. 12. Camera Drawing of an Ultimate Air Passage Division at the Pleura
The dust is deposited at the ends of these more direct passage ways. *B*, bronchiolus in cross section; *P*, pleura. × 30.

Certain observers have been inclined to attribute the dust deposit in lines in the pleura to the relation of this organ to the ribs. It is significant that most of the deposits are on the surfaces that face the ribs. Frequently, too, there is a slight depression in the pleura at the site of the dust deposit which might well represent a depression from the rib. And the ribs, when situated over these areas where dust is prone to become deposited, might reasonably aid, by limiting the movement, for instance, in the deposit. But the fact that black spots and lines do develop on the diaphragmatic and interlobular surfaces where the ribs cannot conceivably have any influence seems to prove that the presence of the ribs is not solely responsible for the deposits.

SUMMARY

1. There are anatomic differences between the lungs of old and those of young guinea pigs. These differences concern themselves chiefly with a larger amount of lymphoid tissue in the older animals. The increase in the amount of this tissue apparently parallels the increase in age and in dust content.

2. Spontaneous pneumonokoniosis occurs in guinea pigs that have lived a cage life for a year or longer.

3. The pigment is laid down under the pleura in spots and lines which mark off the secondary lobules. It is also found in the walls of bronchi and blood vessels, in lymph nodes and lymph masses throughout the lung. In the tracheobronchial nodes it is present in considerable quantity. Practically all of the dust is intracellular.

4. Lymphatics transport the dust cells but these vessels on section usually appear empty.

5. A very slight fibrosis occurs in the tracheobronchial nodes, the pleura and the walls of alveoli that are in the regions of the dust deposits.

METHODS

Numerous fixing reagents were used in this work but the best results were obtained from the use of Zenker's fluid. In general the procedure was to introduce the fixing fluid into the trachea by gentle pressure before the thorax was opened. In this way the tissue was not overdistended.

Sections were made in both paraffin and celloidin, and in many instances sections of 200 microns or more were used to great advantage. There were also free hand sections. Numerous specimens were cleared by the Spalteholtz method.

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THE FOCAL REACTION

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During the course of recent medical history our store of knowledge concerning resistance to infections has been greatly advanced, not only by new methods of research, but by new instruments of precision and by innumerable new discoveries in the collateral fields of science. Immunology in particular gave brilliant aid to both the theory and practice of medicine. The more recent results with chemotherapy, too, are of great value.

There remains withal a definite number of acute diseases that, once established, are still beyond our therapeutic influence, even though our preventive immunization against some of them is effective. When we examine the more chronic infections—granulomatoma, for instance—we must frankly admit that our chief reliance is still the intangible "general resistance," that elusive something which so far has escaped our efforts of exact definition.

Perhaps we have erred to a degree in neglecting to study the reaction of the body to disease—the inflammatory reaction—on a sufficiently broad basis. We have studied separate diseases and local inflammation and partial phenomena, but when one surveys modern medical literature it becomes apparent that the large share that the body as a whole plays in resistance to a pathological alteration, even though seemingly a localized one, is either wholly ignored or our deficiencies in knowledge glossed over under the convenient term "antibodies." "Antibodies," in the strict immunological sense, are by no means the sole factors in resistance, perhaps not even the chief factors in the mechanism.

In the study of inflammation, phagocytosis, the rôle of fibrin, the diluent effect of the fluid exudate, alterations in nerves and blood vessels, local changes in the hydroxyl-hydrogen balance, antibody response (both local and general) and numerous other factors have been considered; but, among the reactions, two that are seemingly of fundamental importance seem so far to have received little attention. These concern (1) the possible activation or stimulation (*Plasmaaktivation* of

Weichardt) of remote cells and organs by products absorbed from the inflammatory focus and (2) the effect which alterations in the permeability of the cell membrane have on increasing or diminishing susceptibility to intoxication.

Recent studies in this direction seem of considerable interest in clarifying our conception of certain phenomena observed in connection with inflammatory reactions; and the studies dealing in particular with the focal reaction might warrant a more detailed discussion, the more so since a number of European papers dealing with the subject have not been generally accessible.

That a pathological lesion, localized in some remote portion of the body, may unfavorably influence a pathological process elsewhere seems logical enough; that a pathological alteration (and this includes induced irritations as well) might favorably influence a coexisting process we cannot so readily accept, yet it is just this fact that we must recognize, study and, if possible, utilize therapeutically. The practice of irritating chronic inflammatory foci in order to bring about healing has been in use since time immemorial. A variety of procedures were devised that ranged from the actual cautery, acupuncture, the seton and the fontanelle, to the milder forms of counterirritation still found in the household even if no longer in the clinic. Curiously enough, measures such as these were in use among all primitive races. Common usage, as well as perhaps occasional successful application, led early to speculation concerning the mechanism of its therapeutic action and a number of fallacious theories were evolved, the scientific refutation of which led finally to complete scepticism concerning the whole subject. But in some form or other we find it cropping out again and again—in the fixation abscess of Fochier and in the autoserotherapy of Gilbert, and clearly recognized in the Bier treatment by hyperaemia.

In the more modern methods of nonspecific therapy we find a more extended effort to make use of the same general phenomenon. But here, just as in former immunological studies, we have given perhaps too much attention to the resistance of the diseased organism to infection, and not enough to the forces that prevent the body from becoming diseased. This Much (1) would designate as nonspecific immunity (*unabgestimmte Immunität*). Morgenroth, Biberstein and Schnitzer (2) have already approached the problem experimentally, in that they have demonstrated that a coincident avirulent streptococcus infection (in mice) will protect from the immediately fatal effect of a peritoneal injection of highly virulent streptococci. Citron and his associates (3) have added their observations with chicken cholera in guinea pigs, in which a subcutaneous injection given just preceding an intraperitoneal injection (normally rapidly fatal) alters the course of the infection, so that merely the chronic type of infection results. I cite these experiments in acute infections in experimental animals merely to illustrate the broad character of the field that is open for study, a field in which the local reaction occupies but a small part.

Ever since the tuberculins were introduced early in the nineties the concept of the focal reaction, the *Herdreaktion*, at the site of the inflammatory lesion has been so closely associated with the diagnostic and the therapeutic principles of tuberculin as hypothecated by Koch that the field has, to a great extent, been limited largely to a consideration of this particular disease. This view of the focal reaction, exemplified, let us say, in a local disease such as lupus or an apical involvement, needs no further elucidation. By some the term, local reaction, is however used synonymously; it should of course be reserved for those reactions that occur at the site of the injection of the tuberculins.

By common consent we may assume that positive local and general reactions are regarded as corroborative evidence that at some time the organism has been infected with tubercle bacilli. To the focal reaction we generally attach greater significance, in so far that the observation of focal disturbance following tuberculin injection is regarded as proof not only of infection but of activity as well. It is regarded as strictly specific in the sense that only tuberculous processes respond to tuberculin injections. On this assumption the immunologists have elaborated theories to picture the processes going on at the site of the reaction. According to Wassermann and Bruck the reaction takes place when the injected tuberculin joins with an "antituberculin" at the focus and complement is bound by these two reacting bodies. The fixed complement is then able to "digest" the focal material and so cause the well known lytic phenomena that we associate with focal activation. Wolff-Eisner and others have expressed the idea that all the tuberculin manifestations are due to preformed specific "lysins." These break up the nontoxic tuberculin; and only the tuberculin so altered can initiate the various reactions. The entire mechanism, according to the humoral views, depends on the presence of lysins, that is, "much lysin—much reaction."

As a matter of fact, little or no evidence has been put forward to support this humoral theory; but, on the contrary, much convincing evidence discredits it. No antibodies of the kind hypotheticated have been demonstrated. Nor does a parallelism exist between the local, focal and general reactions, such as would be predicated if the reaction were a humoral one. On the contrary, while a general reaction follows in the wake of a focal reaction, the local reaction is under these circumstances suppressed. But practically every clinical phenomenon has, nevertheless, been interpreted according to these theories, with resulting confusion. One illustration will suffice. Menzer (4) noted that tuberculous foci would respond with a typical *Herdreaktion* after the injection of a streptococcus vaccine and that tuberculous patients would very frequently have a general reaction. From this he drew the conclusion that such reactions merely indicated that a secondary infection with streptococci had been imposed on the focus and that the evidences of reaction which he observed merely confirmed the specific concept.

It was largely through the demonstration of the focal or *Herdreaktion* that the theory of specificity for the tuberculins gained wide credence. We fitted a theory to the observation, and then proceeded to interpret every clinical observation in this or the related fields to conform to our theory. Reasoning in a vicious circle retarded the study of actual clinical conditions; and particularly held back the proper recognition of certain factors in cellular resistance which are of great importance not only in tuberculosis but in inflammation in general.

Inasmuch as experience with tuberculosis is common to every physician, the consideration of the focal reaction in the tuberculous is perhaps of greatest interest and importance; but the problem is so closely bound up with inflammatory reactions in general that it may be permissible to include certain references to conditions of nontuberculous origin in this discussion.

CONCERNING THE SPECIFICITY OF FOCAL REACTIONS

Perhaps the fact that the focal reaction is not a specific reaction must first be emphasized. Practically every inflammatory focus, irrespective of its etiology, will react (focal activation) to tuberculin, as well as to a great variety of other agents, chemical or biological in character. Workers in tuberculosis have long recognized the fact that the tuberculous lesion responds with a focal reaction to a variety of substances.

Baldwin mentions nucleoprotein, nuclein, albumoses, cinnamic acid, cantharidin, pilocarpin. Fishberg adds potassium iodide and creosote. But the recognition that nontuberculous inflammatory foci will likewise respond to such agents has only been discussed in recent years. Perhaps the paper of Schmidt (5) is of greatest value in this connection in so far as the theoretical consideration of the problem is concerned: his practical deductions are however open to serious criticism, as will be pointed out later.

Schmidt began his observations on the Poncet type of arthritis. This tuberculotoxic form of disease exhibits a well marked focal reaction following the injection of tuberculin; that is, the joint becomes more painful and swollen, there is an increased limitation of motion and the tissues become hyperaemic. This stage is later followed by improvement in the clinical picture (the negative stage is followed by a positive one), the end results usually being an improvement over that obtaining before the tuberculin injection.

But Schmidt found that if, instead of injecting tuberculin, milk was used, he obtained exactly the same reaction at the site of the lesion, during the same time period, and with the same positive phase following in the wake of the reaction (that is, a therapeutic effect). Further, when he turned to nontuberculous joint lesions and injected minute doses (0.001 gram) of old tuberculin (relatively rich in nonspecific proteins) he obtained a similar focal reaction.

CLASSIFICATION OF FOCAL REACTIONS

The German clinicians have gathered considerable data concerning the reactions that follow milk injections (used merely as a convenient nonspecific protein) and Schmidt has arranged the following groups in which there is a response with a typical focal reaction following milk (and other) injections:

1. Inflammatory foci of infectious origin
2. Localized inflammatory processes endogenous or traumatic in origin
3. Diatheses

1. Classified under the first group we include pulmonary foci of tuberculous origin. Schmidt and Kraus (6), Petersen (7), Holler (8), Dollken (9) and others have called attention in recent papers to this phenomenon. Proteoses, iodides, milk, nucleins, among other agents, will bring about a focal reaction and a sharp general systemic reaction. *Tuberculous foci in lymph glands, kidney, genitourinary tract* and elsewhere respond in a similar manner. Closely related we find the effect on *leprous lesions*. Josephson (10) describes the activation of a case of macular leprosy following the accidental injection of a relatively large intravenous dose of vaccine.

Among the nontuberculous inflammatory foci can be included the *tonsils* which at times flare up after a nonspecific injection. Schmidt describes such a case in which a milk injection activated a latent angina with a coincident appearance of mild joint pains. *Furuncles;* inflammatory activation can be observed following milk injections in cases of furunculosis and in some instances more than the usual amount of constitutional reaction. Thus the normal diabetic does not react with a temperature rise to milk injections, but if suffering from furuncles will frequently do so. *Arthropathies;* the negative phase with its increased pain, swelling and limitation of motion is not an uncommon clinical observation and has been fully discussed by a number of observers. *Buboes and adnexal inflammations.* Inflammatory foci in the *appendix and the gall bladder. Erysipelas.*

The activation of quiescent *malarial foci* has assumed diagnostic importance and will be more fully discussed. *Papules of syphilitic origin* react with an increased hyperaemia just as do other inflammatory foci.

In a general way, one can make the statement that any circumscribed inflammatory process, irrespective of its bacterial etiology or its location, will frequently light up with a typical focal reaction after a nonspecific injection, and that usually within twenty-four hours after the injection. Of these various processes tuberculous lesions are perhaps more sensitive because of a more profound sensitization of the tissue cells of the host *against protein in general*, as suggested by a recent discussion by Wolff-Eisner (11).

2. Localized inflammatory processes endogenous or traumatic in origin. In this category must be placed certain of the *toxic forms of arthritis*, such as the Grocco-Poncet type; *inflammatory lesions of the kidney;* inflammatory lesions of the eye, including iritis, albuminuric retinitis, etc. Healing fractures, such as Dollken has described, respond with a typical focal reaction.

3. Localized lesions on a basis of a diathesis. Using this term in the broader significance as defined by Pfaundler, the following conditions might be included:

The *lancinating pains of tabes* which at times follow nonspecific injections, as well as an occasional gastric crisis.

In *general paresis* the psychic state may be decidedly disturbed and the disease manifestations become more apparent following nonspecific injections. This is a not uncommon experience in the treatment of paresis, as outlined by v. Jauregg. In *epilepsy* an attack may be inaugurated if a large dose of a nonspecific agent is administered, just as in chronic alcoholics an attack of *delirium tremens* may follow such an injection.

In this sense we may consider that a latent symptomatology may abruptly unfold its various manifestations following injections.

ACTIVATING AGENTS

We must for a moment stop to consider the agents that are involved in eliciting this nonspecific reaction. Because of the early work in this field we commonly regard the nonspecific reaction such a one as follows the intravenous injection of a vaccine, for instance, typhoid vaccine, or such protein derivatives as proteoses, or, more recently, the use of milk or casein given intramuscularly. Not only do such injections bring about the reaction and focal activation, but certain general biological alterations, such as coincident but remote disease processes. Metabolic alterations and alterations of endocrine origin, fatigue, intestinal intoxication, blood-letting, X-ray exposures, trauma, alterations in the skin (counterirritation), as well as a number of drugs bring about exactly the same focal alteration. The activation of a tuberculosis by an angina, a remote trauma, the menstrual cycle, by influenza or measles; the provocation of a malarial paroxysm (the result of a splenic focal activation) by an intercurrent disease, by prophylactic vaccination, by severe fatigue, long railroad journeys, overheating, exposure to intense light, chilling or drenching, dietary faults, alcoholic excess and the various other factors that the experience of the war has brought to light; the activation and focal reaction about latent arthritic lesions such as Pemberton has pointed out (by raying, radium, thyroid extract, excitement, etc.); the classical activation of gonorrhoeal processes by a variety of seemingly remote causes; the precipitation of lancinating pains or a tabetic crisis following a "cold;" the origin of a delirium tremens following a trauma; these are but a few examples of a universal phenomenon heretofore commonly observed but not recognized as having a common background.

A BROADER CONCEPTION OF THE FOCAL REACTION

It is very probable that many puzzling clinical manifestations and unusual features of certain diseases may readily be explained and will appear in a very simple light if we keep in mind the basic idea that the particular symptom complex under study may be due solely to the activation of an inflammatory focus of exogenous or endogenous origin in the manner of the *Herdreaktion.* Many of the curious metabolic disturbances at times associated with diabetes and nephritis can readily be accounted for on such a basis. Even pharmacological study reveals evidence of this same nonspecific effect on inflammatory lesions. Thus, the commonly observed Jarisch-Herxheimer reaction (the flaring up of syphilitic skin lesions under specific treatment) is an example, while the activation of a tuberculous lesion after iodide medication is an even older observation. So too, we may get an ulcerative catarrhal condition when an uraemic colitis is carelessly treated with calomel; while Königer (12), in a recent paper, has even been able to demonstrate that the antipyretics given in proper interval doses, all bring about a nonspecific *Plasmaaktivation* and must therefore be included among those potentially capable of bringing about focal reactions.

This widening of the concept of the focal reaction makes it of decided importance in the special pathology of internal diseases. Acute conditions may often be nothing more than the exacerbation of heretofore latent processes of definite bacterial etiology or perhaps of a diathesis. On this basis can be explained the fact that children often respond with a severe angina to a fault in the diet; that an appendicitis will become acute following an angina, a remote trauma or an injection of a prophylactic dose of vaccine; or that a gastric crisis or lancinating pains will commence after some remote exciting cause or an asthmatic attack occur under the influence of some meteorological or climatic alteration.

In many ways this basis for the immediate etiology of an appendiceal inflammation or the flare up of a gall bladder infection seems more rational than the suggestion that we deal with a specific localization of bacteria, so altered in their metabolic demands and peculiarities that they will grow only in certain tissues. This latter hypothesis, which Rosenow (13) has developed, ignores the fact that in the history of acute inflammatory processes one may note a preceding history of remote trauma or systemic shock of some kind or a metabolic disturbance of nonbacterial origin, just as often if not more frequently than a history of a preceding infection.

THE DIPHASIC CHARACTER OF THE FOCAL REACTION

While in the preceding pages attention has been centered on the fact that a variety of agents may be used to elicit the tuberculin reaction (focal), one can also determine that nontuberculous processes respond with a focal reaction to tuberculin. Schmidt illustrates this with two convalescent cases of polyarthritis which had been free from fever and local symptoms, pain, etc., for over two weeks. Both cases on receiving 0.001 gram, O. T., subcutaneously, responded with severe pain in the joints previously involved, slight periarticular swelling and some limitation of motion; the duration of the reaction was of course transient. I have had occasion to repeat these observations of Schmidt's and in a considerable percentage of the cases studied I have found that the observation holds true. In processes that can be observed at the external surfaces of the body, particularly in the violent activation of chronic inflammatory lesions, one can observe the dualistic nature of the reaction—and this is of paramount importance in its therapeutic application—a negative phase in the sense that the tissue is altered more from the normal than heretofore, that is, the evidences of inflammation are increased, pain and swelling augmented, function impaired, etc.; then a positive phase during which there is a progressive diminution of the inflammation until the preinjection status is again reached or passed, the balance swinging in this direction until practically normal conditions are restored. Augmentation of the inflammation is followed by a diminution until healing is accomplished—the pendulum swings from one side to the other in the wave like curve that we find expressed so commonly in many biological processes—in the opsonin curve, the antiferment curve, in the leucocytic response, in the coagulation mechanism, in cell permeability, all indicative of the exquisite lability of the balance that exists in living protoplasm.

This diphasic alteration of the pathological picture comes to notice particularly in the arthritic focal reactions where soon after the provocative injection (typhoid bacilli, milk, tuberculin) there can be observed increased pain, redness, and swelling and limitation of motion, followed by an analgesia, a lessening of the swelling and restitution *ad integrum.* By way of the circuit of an increase in inflammation we reach the therapeutic goal of a restoration to normal.

The focal reaction has its counterpart in the general reaction of the patient that usually accompanies the reaction, occasionally in the tuberculous, more often in acute infections. Let us examine the reaction that follows when a typhoid patient is injected with vaccine or milk or proteoses or other nonspecific agents which in the normal individual cause little or no reaction. Following the injection there is first an intensification of symptoms, subjective as well as objective. A chill, a rise in temperature, an increase in pulse rate, gastrointestinal engorgement with occasional nausea and vomiting, increased tendency to hemorrhage, occasionally increased mental impairment, delirium, etc. Subjectively the patient complains of headache, chilliness, lassitude, general muscular and joint pain. The course now changes and the positive phase sets in. When the headache ceases the patient usually falls into a profound sleep, the temperature comes to normal either temporarily or permanently, the pulse rate is lowered and the quality becomes better, the sensorium is clear, the patient feels well. During the course of the next day or two the rose spots fade, the splenic tumor recedes, the diazo reaction becomes negative. The blood culture may or may not become negative, shortly after the injection. This period corresponds obviously with Weichardt's period of *Plasmaaktivation*. This duality observed in both the focal reaction and the general reaction is of utmost therapeutic interest.

It is reasonable that we would seek to make the negative phase, representing an augmentation of the inflammatory process, as short as possible and the positive phase relatively intense and protracted. But the possibility arises, based on clinical observation, that the degree and extent of the positive phase (curative) is closely dependent upon and correlated with the negative phase, that is, that their relative intensity is proportional. We may conceive the negative phase, which in point of time always precedes the positive one, as an exogenously produced irritative process; the positive one, on the other hand, as an endogenously prepared, more or less physiological process of vital repair. Clinically, as far as focal reactions are concerned (as for instance in tuberculosis), it is chiefly the negative phase that comes to our attention, in the form of the activation phenomena with which we are familiar. But from the analogous studies in focal reactions elsewhere it must be assumed that with proper dosage, the positive phase and the increased tendency to healing follows about the lung focus just as it does about a joint lesion which can be objectively studied. In this duality of the reaction lies the usefulness of the focal reaction as a therapeutic measure.

THE MECHANISM OF THE FOCAL REACTION (VASCULARIZED INFLAMMATORY FOCI)

During the course of the past five years we have become familiar with the biological alterations that take place in the organism after tuberculin injections, as well as after so called nonspecific agents. These changes are numerous and complex but the more important can be placed in two groups, (1) those that deal with cellular stimulation and those (2) that result primarily from alterations in the permeability of the cells.

The former have been broadly included by Weichardt under the term *Plasmaaktivation.* Under the stimulus of moderate doses of nonspecific agents cellular activity is markedly increased. This finds its expression in increased secretory activity of gland cells, increased activity of muscle cells (myocardium), increased activity of leucocytes (phagocytosis), etc. The changes that take place in the permeability of the cell membrane have been studied by Luithlen (14), by Starkenstein (15), and others, and represents a decidedly diphasic phenomenon. The permeability of the capillaries is first increased as evidenced in the great increase in the lymph flow and in the concentration of the blood; the permeability of the tissue cells is increased—with a resulting outpouring of enzymes, of fibrinogen and prothrombin, of immune bodies, etc.; the increased permeability of the nerve cells is associated with a lowering of the threshold for nervous impulses and becomes manifest clinically in increased susceptibility to pain, general irritability, headache, etc. When this first phase has passed, compensation takes place in a lessened permeability of the cells, with effects that are to be anticipated—lessened susceptibility to intoxication, lessened nervous irritability, lessened exudation, a lowering of enzyme concentration, etc.

Numerous other observations have been made that are, in my opinion, subordinate in interest to these two fundamental alterations in the permeability of the cell membranes and the general stimulation of protoplasm.

With these considerations in mind we can approach the study of the mechanism possibly involved in the focal reaction about inflammatory tissues from a relatively simple point of view.

In an inflammatory focus, supplied with highly vascularized granulation tissue, the systemic effects of a tuberculin injection or the injection of a nonspecific agent will bring about (1) an increase in the exudation of fluids, with increased redness and swelling, because of the transient increase in the permeability. With this there is associated (2) an increase in pain and tenderness both because of the increased pressure and the lowering of the threshold of nerve stimuli. There will be (3) increased digestion at the focus of inflammation; if there is no necrotic material present in the focus there may be no evidence of increased systemic intoxication; if the amount of necrotic material is large there will first result an increase in systemic intoxication when the material split down is absorbed, and with more complete digestion at the focus complete detoxication may result.

All these changes we associate with the focal activation that follows nonspecific injections. To these must be added another factor and one more complex. It concerns the observation that any cell previously involved in an inflammatory reaction responds to stimuli of all kinds more readily than a normal cell. Objectively we can observe this in involuting skin lesions.

From the immunological point of view the work of Conradi (and Bieling (16) and Bieling (17) is of interest in this connection. They have found, for instance, that if a rabbit is first immunized with typhoid bacilli, the dosage of bacteria needed to bring about a high degree of immunization against some other organism—cholera, for instance—is only a fractional part of that required to immunize a normal rabbit. This alteration in immunity response, which is, of course, omnicellular, merely illustrates the alteration in reactivity that we find in the epidermal tissues, and very likely in inflammatory tissues in general.

The augmentation in the inflammatory reaction which we have induced brings with it as we have seen an increased lymph flow. Coincident with it there has been a relative increase in enzymes,—proteases, ereptase (peptidase), lipase, etc.—an increase in the antibodies (if the patient has been previously immunized or if the infection has existed for some time) and an increase in the leucocytes (after the initial leucopenia), together with an increase in their phagocytic activity and an increased coagulability of the blood. The antibody, the leucocytic and the enzyme alterations must exert a considerable effect on an infecting agent as well as on the removal of necrotic material; the tendency toward restitution to the normal would be enhanced. It is this phase that we see in the so called second or positive phase. Its coincident constitutional effect that we witness in the euphoria, the lowering of the temperature, the improvement of the circulation, etc., is due to at least three factors: (1) the destruction of toxic material at the focus after the primary increase in digestive activity, (2) lessened susceptibility of the cells of the body to intoxication (due to the lessened permeability), and (3) actual protoplasmic stimulation (from the nonspecific or specific agent injected, partly from the toxic material liberated from the inflammatory focus). This latter factor varies greatly and the clinical estimation of the possible degree of this variation requires experience and care.

TUBERCULOUS FOCI

If we turn now from the vascularized inflammatory focus to the tubercle, other conditions confront us. In Schmidt's paper we find the view emphasized that in the general tuberculin reaction we are most likely dealing with both specific and nonspecific factors, an opinion similar to that which we expressed in a previous paper (7). Schmidt had stated this concept as follows:

> But it is probable that in the question of specificity *or* nonspecificity the placing of the one versus the other is a mistake—that it should rather be the examination of specificity *and* nonspecificity, that is, that both factors enter into the reaction and it should be determined how far each factor is involved.

Our concept has been that while the systemic reaction was largely nonspecific in that the means used to elicit it need not be specific, the focal reaction itself, once initiated, brings in its wake a truly specific stimulation because the inflammatory reaction may lead to the liberation of disintegrating bacterial material and possibly even living bacteria. These substances would secondarily lead to a specific response on the part of the body.[1]

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[1] It is this factor that Klemperer (18) in his recent criticism of Schmidt's claims has ignored. Klemperer found that following milk injections in tuberculous patients they did not become resistant to following injections of tuberculin and vice versa. Injections of milk bring about a febrile reaction in a large percentage of individuals, and a focal reaction in only a limited number of tuberculous patients, just as tuberculin injections are followed by focal reactions in an irregular number. If the injection of milk brings about (in the tuberculous individual) a systemic reaction without focal activation, a following injection of tuberculin may still give rise to a typical general reaction. If, on the other hand, a focal reaction results, either by specific or nonspecific means, local tuberculin reactions are suppressed for some time following the general reaction. Klemperer is however quite justified, both in his criticism of the local reactions reported by Schmidt following milk injections in tuberculous patients and in his views concerning the possible harm from activation of tuberculous foci following milk injections.

At least three factors must be considered in the mechanism of the focal reaction in tuberculosis, apart from the anatomical peculiarities of the tubercle as contrasted with other inflammatory processes.

Specific. These concern primarily a tissue sensitization against tuberculoprotein, strictly specific in character, cellular in its localization and not necessarily associated with the older conception that was built up about the humoral antibodies. Indeed, I am of the opinion that the latter may very well be relegated to a subordinate position in the field of tuberculosis. Inasmuch as this subject of tissue sensitization has been extensively discussed by a number of workers, particularly by Krause in this country, it will be unnecessary to enter into this phase here.

General hypersensitiveness of the tuberculous. Granted that the tuberculous focus responds to smaller doses of tuberculin than does a focus of nontuberculous origin, how are we to account for the fact in view of the practical avascularity of the tubercle? That the specificity concept of the immunologist will no longer explain the accumulated evidence is to-day acknowledged and Wolff-Eisner accepts the change in our viewpoint in a recent paper (11). I can but very briefly enter into the more lengthy theoretical discussion that he presents. He first emphasizes the relation that exists between the diet and exudative diathesis, defining this latter condition as due to the absorption of proteins and protein fragments insufficiently degraded in the intestinal tract, that is, a protein sensitization. He then develops the more or less definite association of the exudative diathesis and spasmophilia with scrofula. While he does not regard the scrofula as the cause of the diathesis, he inclines to the definition of Feer that "scrofula is tuberculosis on the basis of exudative diathesis (19)." Wolff-Eisner is inclined to the view that in tuberculosis there is evidence of an exudative diathesis with sensitization against tuberculin and also *against proteins in general.* This latter, which is nonspecific and general in character, accounts, in his estimation, for many of the evidences of similarity in the clinical course of tuberculosis and those observed in an exudative diathesis. Not only is scrofula "tuberculosis on the basis of a diathesis" but the tuberculous lesion itself, involving as it does the prolonged absorption of partially split proteins from the necrotic foci, may ultimately bring in its train symptoms that are commonly regarded as due to a diathesis. As such, he regards the changes observed in the cornea, skin lesions such as the tuberculids, and the decided alterations in the reactivity of the sympathetic and central nervous systems to which Moro, Pottenger and Ferranini have called attention. While we have been familiar with the increased nervous lability of the tuberculous individual for a long time, we have failed to grasp the dependence of the increased irritability on the general hypersensitiveness to proteins. Not only does this nervous irritability indicate the close parallelism to the diathesis of the child, but the tendency to effusion is also evident in the tuberculous patient: one has but to call to mind the common appearance of pleural, peritoneal and joint effusions. The alteration in the vasomotor stability also finds its expression in the frequent appearance of urticarial eruptions after tuberculin injections.

It will be recalled from the previous discussion of the effects of nonspecific injections on the permeability of vascular endothelium that, depending on the dosage or the degree of irritation (or stimulation if we wish to use that term), there may result either an increase or a decrease in permeability. We may expect that the effect of the tuberculin (or the living virus) will also find some expression in changes in permeability in one direction or the other. According to Wolff-Eisner we find the clinical demonstration of this experimental observation in the effect of the tuberculous invasion of lung tissue, where in one instance we find an exudative change, in another an indurative process.

Plasmaäctivation. The third factor involves the consideration of the effects which any nonspecific provocative agent would have on an inflammatory lesion such as the tubercle. The tubercle would react as any seminecrotic focus of other etiology would react, were it not for the fact that the tubercle is practically avascular. Tubercles react to nonspecific injections (or to nonspecific stimuli of other origin) only when they are of the exudative type or when the connective tissue delimination of the tubercle is either incomplete or exceedingly labile. It is to be recalled that, as one of the results of plasmaäctivation, proteolytic enzymes appear in the serum and in inflammatory foci and that the polymorphonuclear leucocytes are increased in number and in activity. The augmented digestive activity results in a loosening of the connective tissue defense of the tubercle. If sufficiently intense a typical focal reaction (activation, absorption of necrotic material, and systemic reaction) can result in this way, just as after stimulation due to specific tuberculins.

THE THERAPEUTIC APPLICATION OF THE FOCAL REACTION

Schmidt is of the opinion that the focal reaction, elicited by means of specific or nonspecific agents (milk), is of definite value in tuberculosis and together with Krauss cites some twenty odd cases to support his view. While it is of course not to be denied that in a very limited number of cases this may be true, we are of the opinion that the tubercle offers a decided exception to the general rule that the active stimulation of a chronic inflammatory focus is of therapeutic value. We have pointed out that for vascularized inflammatory lesions such stimulation affords a rational method of therapy. In the tubercle we deal with the constant danger that the limitation of the lesions, by means of the connective tissue encapsulation, may be sufficiently disorganized, so that an extension of the process and irreparable injury may result. Irrespective, therefore, of the theoretical probabilities that therapeutic focal activation may be beneficial, in the tuberculous lesion it is a hazardous procedure. Before leaving the subject it must be pointed out that nonspecific stimulation of the tuberculous patient (not involving local reactions) has been found very useful, both with certain drugs (and these include the commonly accepted ones such as creosote, succinides, arsenicals, etc.) as well as with serum injections such as Czerny and Eliasberger have recently reported (20). That the milder nonspecific injections seem to have a decidedly stimulating effect on the metabolism of infants has been previously reported.

The peculiar therapeutic importance that attaches to the diphasic character of the focal reaction has been previously discussed. Through the existence of inflammatory foci in various organs the omnicellular stimulation, by means of the various nonspecific agents (the ergotropie of v. Groer), becomes to a certain extent an organotropie. It is in this sense that we must consider the effect of the treatment of general paresis by means of tuberculin injections and similar therapeutic measures. A combined therapy of nonspecific and aetiotropic agents may be of value and experiments in this direction have been reported by Kyrle and Scherber (21) who have used milk injections in conjunction with mercury in the treatment of syphilis, or the use of milk injections and salicylates in the treatment of arthritis, the use of milk injections and luminal in the treatment of epilepsy, or the treatment of lupus with tuberculin and salvarsan (the latter in this case serving as the nonspecific agent). Our older method of treating syphilis with alternating courses of mercury and iodides made use of this form of a combined specific and nonspecific method for many years. The nonspecific effect of the mercury is, however, not marked. The effect is to be sought rather in the effect of the iodides in facilitating the diffusion of the mercury. If a more active agent than iodide is used the mercurialization of the patient can be very rapidly brought about.

SUMMARY

In view of the demonstrated fact that tuberculous foci may react to nonspecific stimuli and conversely that nontuberculous foci may react to tuberculin, the fallacy of the purely specific concept of the focal reaction is discussed. Focal reactions can be classified according to the Schmidt scheme as those that occur (1) about inflammatory foci of infectious origin, (2) about localized foci endogenous or traumatic in origin and (3) on the basis of diathesis. Such reactions take place not only after specific stimulation, but after a wide variety of biological alterations in the organism. This widened concept of the focal reaction would seem to make clear a number of common clinical observations, such as the flaring up of gall bladder, appendiceal, arthritic or other localized inflammatory foci after remote trauma, vaccination, gastrointestinal disturbance, X-ray exposure, fatigue, chilling, etc.

The focal reaction, no matter how elicited, is essentially a diphasic phenomenon, consisting in an augmentation of inflammation, followed by a diminution, and a tendency to complete restoration to the normal. In a general way it may be stated that the second phase (positive or healing) is closely related to the intensity of the first (or negative) phase, that is, the more intense the inflammatory reaction, the greater the tendency to a complete restoration to the normal. In this phenomenon lies the therapeutic usefulness of the focal reaction.

In the mechanism of the reaction two general factors have heretofore been largely ignored. These include the effects of the (1) so called *Plasmaaktivation* (Weichardt)—an omnicellular stimulation by means of proteins, protein split products and a large number of other substances—and (2) the alteration in the permeability of cellular membranes (with vascular, nervous, glandular and other effects).

In the mechanism of the focal reaction in tuberculosis at least three factors are involved: (1) a true and strictly specific sensitization of the organism, (2) a general hypersensitiveness of the organism against proteins and (3) a nonspecific reaction about the tubercle. This latter is of course greatly modified by the anatomical peculiarities of the tubercle (avascularity, encapsulation, accumulation of necrotic material, resistance of the tubercle bacillus, etc.). Schmidt's deduction that focal activation in tuberculosis may be beneficial, while theoretically defensible, is clinically unwarranted because the reactions are beyond our control and the digestive processes incident to the reaction may destroy protective connective tissue and result in the dissemination of the disease.

In the therapeutic application of the focal reaction in nontuberculous disease, attention is directed to the fact that favorable results have been reported from combined nonspecific stimulation and the use of aetiotropic agents. Thus milk injections and mercury (in syphilis), tuberculin and mercury (in general paresis), milk injections and salicylates (in arthritis), milk injections and luminal (in epilepsy), salvarsan and tuberculin (in lupus), etc., have been reported in this connection.

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THE IMPORTANCE OF SUBLIMINAL SYMPTOMS AND PERIOD OF ALTERNATION OF REST AND EXERCISE IN THE TREATMENT OF PULMONARY TUBERCULOSIS

HENRY SEWALL

To one whose memory covers an interval of fifty years in the application of methods for the prevention and cure of pulmonary tuberculosis human endeavor resembles the up and down motion of waves upon the sea. A floating chip would seem, like a pendulum, to get nowhere, however violent its oscillations. But careful observation shows that there is not a fleeting wave but translates the chip minutely in a definite direction, until in time it helps to build the solid coast.

Fifty years and more ago, vigorous physical exercise and abundant pulmonary ventilation were the favorite prescriptions of most who ventured to advise the ailing ones suspected of tuberculosis. A much exploited utensil for pulmonary ventilation was a breathing tube which could be carried in a vest pocket. Inserted between the lips, air could be freely inhaled to deepest inspiration, but a valve opposed its free exit so that the expiratory movement must have sensibly increased the intrapulmonary air pressure. There could have been no atelectatic collapse under such conditions. No doubt many a useful life owed its years to such a regimen; but it is more than credible that a silent majority mutely suffered the disaster of exercise out of season. Even to-day the thoughtful practitioner must often confront the homicidal therapeutics left over from that era.

Then, about the middle eighties, the importance of physical and mental rest and of the open air life gripped thinking minds, and the remedial powers of these measures were worked out in therapeutic laboratories—sanatoria.

Then tuberculin began its checkered career of riotous living. It, and the vaccines, and now the proteoses, are edged tools which always merit fear, sometimes respect.

Of recent memory is the brief period of superalimentation, when the gain of body weight on the part of a patient was supposed to hold a direct proportion to his vital well-being.

These salient phases in the evolution of tuberculosis therapeutics are mentioned because undoubtedly each had specific value in our conflict with disease.

The present essay is intended as a modest inquiry into the question as to whether we are not now in a position to perceive more clearly than before the meaning of tuberculous phenomena, to winnow the chaff from the wheat in the harvest of therapeutic experience and to deploy more systematically than hitherto the useful data of experience in our treatment of pulmonary tuberculosis.

To my mind, the most outstanding rational exposition of the forces at work in a clinically tuberculous subject is that made ten years ago by Marcus Paterson (1); his conclusions then expressed have recently been reaffirmed in their logical consequences (2).

Paterson minimizes the importance of the anatomic lung lesion and magnifies the value of pathological intoxication emanating from it. Our hard earned skill as adepts in physical diagnosis he would implicitly relegate to the academic realm of cultural training. At all events, he would eschew, as far as possible, all physical examinations, after diagnosis has been made, on the ground that they may cause excessive mobilization of injurious toxins. Can it be doubted that we ourselves sin repeatedly in this regard in our eagerness to trace the course of infections? Have not surgeons luminously demonstrated that toxic material when confined is harmless, but when transferred to the circulation by whatever means, of which the commonest is mechanical pressure or motion, it is fraught with danger to the living cells?

The essential fact disclosed in every useful record of experiment or experience is that the one dominant condition in tuberculosis is intoxication. Intoxication causes, by and large, all the constitutional symptoms of the disease; and, moreover, wonderful to say, it is the essential stimulus that awakens the antagonism of protoplasm to resist the disease. We must not be afraid of platitudes. Truth is like an object viewed through the microscope; only in a single plane of vanishing thinness is it clearly in focus; or it resembles an image on the periphery of the retina, good enough for rough perceptions but useless for exactness until brought upon the fovea. The writer feels that this itself is a great truth, since his own experience is full of images which for years were mistakenly thought to be clear but which were really obscure, seen through a glass darkly, and which now and then suddenly take on a sharpness of definition that gives them usable precision.

There cannot be one truth of the laboratory and another of the sick-bed. The real facts from each arena must match like the blocks in a puzzle. The opinion may be ventured that the rational treatment of tuberculosis depends upon a workable understanding of those tissue responses to intoxication which are characterized as sensitization, desensitization, anaphylaxis and immunity. Though we know some of the conditions of their occurrence, we are far from knowing what they are. Only in the laboratory can we properly gain an experimental knowledge of their meaning; incidentally in passing, it may be suggested that such practical study should be a torch to light the practice of every physician.

The practical student of tuberculosis must be equipped with a working theory if he would systematically help others and, above all, if he would help himself to understand. To-day the rubric of his faith is *Intoxication*. Herein is the applied energy of infection through which all its good or harm to the body is mediated. No day passes but brings to the observer new and astounding evidence that infection is the chief genius of clinical pathology, which must be identified and located in order to be subdued.

None but he who himself has harbored an active focus of infection can truly grasp the varied power of toxins to plague the soul or cripple the body of man.

If we but grant that the disease, tuberculosis, wreaks its harm through accession of specific toxins to the circulation, our clinical study primarily reduces itself to the recognition of the symptoms of intoxication. Invaluable for this purpose is the universal, if crude, method of estimating the body temperature by the clinical thermometer. As to the technique of the procedure, the writer would maintain that for ordinary use the record obtained from the mouth is good enough. It will here be assumed that for purposes of treatment no rise of temperature is so minute but it deserves attention. This would seem to necessarily follow, if we concede the truth of all modern teaching that the subjection of tuberculosis is easy in inverse proportion to the duration of its existence.

The writer's individual studies have sought to penetrate the clinical history of the tuberculous patient to a biological period far antecedent to the gross changes crudely indicated by the clinical thermometer. Every patient is apt to develop a chain of specific morbid symptoms which announce his own subjection to tuberculous intoxication. It seems to me that the individual study of each patient for the detection of his own peculiar symptomatology is an important, perhaps the most important, duty of the clinician.

It would greatly advance tuberculosis therapeusis could some one categorically define what, for lack of a satisfactory adjective, may be called the "subliminal" evidences of tuberculous activity. In another place (3) I have urged that it is possible to detect a constitutional functional disability of a very large group of near-invalids, especially through study of the blood pressures, people who still can pursue a vocation but in distress and without savor. Analysis of the appropriate cases shows them to suffer from infection of some kind, and from my own list of several hundred subjects most of them who manifest the symptoms disclose to X-ray and properly conducted physical examinations the evidences of pulmonary organic changes similar in kind to those found in the lungs of the demonstrably tuberculous.

A large and important group which is not definitely recognized, important because its victims usually consist of people of high intellectual organization, may perhaps be best typified by a definite example: A man on the sunny side of forty, of high accomplishments in his profession, one of absorbing interest and activity, began some eight years ago to show signs of breakdown. He recuperated fairly well under a period of rest, but return to work again sapped his powers, and the clinical history was one of alternate break and repair with gradual mean deterioration throughout the years. Examination of the lungs showed evidence of active tuberculosis and the sputum developed tubercle bacilli. When, for the first time, the pathological condition was fairly grasped, a few weeks' bed rest and a few months' graduated exercise on alternate days removed all the characteristic symptoms of tuberculosis. There was great gain in weight; normal temperature; vanishing, bacilli-free sputum; and a delightful sense of well-being and great improvement in nervous stability. Excessive exercise still takes too much out of him and undue use of the eyes is apt to be attended with headache. Radiograms of the lungs indicate pronounced development of fibrosis. Can this man safely return to his work and how soon? This athletic subject, of medium height and weighing 180 pounds, has a maximal blood pressure of 95 to 105 mm. Hg. In the supine position his pulse pressure maintains the low standard of 30 to 32 mm., while standing erect it falls to the near-shock level (Erlanger) of 15 mm.; at the same time there are perturbations in the diastolic pressure which suggest vasomotor disturbance. My conclusion is that the brain is underfed in the standing posture, and that this anaemia, if imposed upon, will inevitably lead to somatic failure. Some regimen must be devised through which the mechanisms of the circulation shall be able to achieve and maintain their coördinations.

A definite study of this question for more than ten years has convinced me that so simple a test of constitutional reaction-power as the comparison of the arterial blood pressures in the recumbent and erect postures often gives the key to failures in physiological resistance which are otherwise inexplicable.

Another highly intelligent patient, whose career has provided a rich fund of clinical information, a young man whose disease activity could be controlled only by the induction of artificial pneumothorax on the right side, has been able to grade his symptoms somewhat according to the degree of intoxication while the latter is still not indicated on the thermometer.

These symptoms are more or less completely allayed after injection of air into the chest but after a period of about ten days they reappear and tend to progress with increasing intensity. Through them it has been possible to settle on the most favorable interval for air injection, which has been, for some time past, ten to twelve days. The symptoms in question are increased cough and expectoration; indigestion, attributable to hyperacidity; a feeling of malaise; a diminution of vital energy, described as loss of "pep;" a strained or bilious feeling in the eyes; aching pain in the shoulders; finally an actual rise of body temperature appears and the patient feels ill.

Observations upon this patient suggest that there is a very exact quantitative relation between the intensity of intoxication and the clinical expression of symptomatology. Perhaps it is not necessary to say that the special therapeutic resort in the amelioration of these, as of other symptoms of auto-inoculation, is absolute rest in bed. In an investigation now being conducted in collaboration with Dr. S. Swezey, we find that tuberculo-intoxication is manageable to a considerable degree through regulation of the mobility of the costal parietes, and we have been convinced by experiment of the truth of the great conception that the management of tuberculosis depends upon the control of auto-inoculation.

The theoretical phthisiologist and the tuberculosis specialist unite in the preachment demanding earlier diagnosis of tuberculosis. If an exact schedule could be drawn up showing the biological symptoms significant of developing tuberculosis, its publication would probably meet with much the same popular reception as did Noah's warnings of the Flood: "For the rain it raineth every day," so why waste thought over any particular rain?

Abandoning metaphor, it is intended here to advocate the definite apprehension, study and treatment of slight symptoms in cases of proved tuberculosis of unstable vitality; and especially in the persons of those who, for reasons of heredity, environment or idiosyncrasy are supposedly especially liable to develop the disease. Every clinician who has led a tuberculous patient to an arrest of his disease dreads the hazards involved in his return to former occupation amid his old surroundings. It may be contended that the all too common fatal relapse of the seemingly restored invalid who ventures to resume the normal life might often be averted were he carefully instructed as to the nature and treatment of the "subliminal" symptoms of his disease. The nice discrimination of tuberculosis (significant symptoms amid the indifferent swarm of similar quasipathologic manifestations) is an important aim in the physician's education. Far from increasing the complexity of our problem, however, such a method simplifies it. The physiologist who experiments with a living apparatus finds that its reactions become more mechanical and predictable the more exact is his control of the experimental conditions; successful scientific research transmutes mystery into mechanics.

ON ALTERNATION OF REST AND EXERCISE IN THE TREATMENT OF TUBERCULOSIS

We must now take up an ambitious theme, a consideration of the quantitative relations between physical exercise and tuberculous activity.

As has been pointed out, it was the great merit of Marcus Paterson to clearly grasp the idea that clinical tuberculosis is merely a function of tuberculo-intoxication. Progress of the disease is due to the presence in the circulation of an amount of toxin in excess of the ability of the tissues to destroy by physiological reaction. Such toxemia is recognized by multifarious symptoms, of which fever, though late in the chain of effects, is most easily apprehended. The first phase of any course of treatment has the aim of reducing intoxication below the threshold of pathological disturbance. This purpose to-day is accomplished by physical and mental rest, whose most efficient influence probably depends upon lessened circulatory activity in and absorption from the tuberculous foci.

Right here it seems expedient to point out that Rest as opposed to Exercise, is not a mere negation, as darkness opposed to light. The physiologist admits two great phases of vital power; one, kinetic, chemically katabolic, energy evolving. The other is Inhibition, manifested by restraint or cessation of activity; often or always chemically anabolic, energy accumulating. The known relations of Inhibition to Activity are far from complete solution but, though we still fail of a comprehensive definition of the former, we must grant that the one entity is as real as the other. There can be no doubt that as toxemia reaches its irreducible minimum through absolute bed rest, the forces of physiological reconstruction in the body are hard at work repairing damage and storing power. It is no vain analogy by which the results of rest in disease suggest those of inhibition in health.

But cure of disease and return of the patient to useful occupation cannot be achieved except through an active chemical conflict between the tuberculo-toxins and the tissues, in which the latter are so far victorious as to maintain a structure competent for physiological efficiency. The prime object in the treatment of the tuberculous patient is, then, to feed his tissues with an amount of toxin which is well within their power to assimilate, neutralize, destroy, or what not.

Paterson accomplishes this purpose through his well known graduated muscular exercises. Certain personal experiences, some three years ago, led me to the conclusion that in a considerable group of refractory subjects the induction of exercise could be applied more safely and effectually by spacing the exertions on alternate days. The idea was the outcome of experience with a young man who carried a sharply circumscribed tuberculous consolidation in the upper right lung. With bed rest he was symptom-free, but when allowed a daily visit to the bathroom and toilet there followed on the third day a sharp rise in temperature; and simultaneously moist râles appeared not only around the tuberculous focus but in the sound lung as well, and the patient felt ill. He was quickly restored under complete bed rest, but the experience was repeated many times within a few months. The therapeutic test with quinine seemed to show that the paroxysms were not malarial in origin, and the Widal reaction was negative for typhoid fever. Reflection upon these data led to this conception: The exertions of the first day's visit to the bathroom mobilized tuberculo-toxins which sensitized, or resensitized, the body tissues, but led to no obvious interference with normal metabolism. The exertions of the second day accentuated these disturbances and by the third day the hypersensitiveness of the tissues was so increased that an amount of toxin previously inoperative caused an "anaphylactic" explosion. In the terminology of Almroth Wright, each dosage of tuberculo-toxin was given during the "negative phase" produced by the preceding dose. It seemed obvious that the proper way to treat this case was to act on the realization of the fact that the exertions of the first visit to the bathroom actually produced a general metabolic effect, though this was not manifested by symptoms. The living cells require time for the elaboration of their reactions. Given sufficient time the metabolic wave set up in the tissues by the tuberculous antigen will progress from the trough of hypersensitiveness to the crest of specific resistance. The "negative" is followed by a "positive" phase. Experiments on the guinea pig which will shortly be mentioned, have led me to think that forty-eight hours, commonly, is the interval necessary to complete the metabolic wave. That is to say, in order to summate tissue resistances rather than tissue hypersensitiveness, successive inoculations should, in appropriate cases, be spaced at intervals of forty-eight hours. This conception was at once put in practice on a tuberculous subject who for nearly twenty years had been the despair of my therapeutic management. Graduated daily exercise for him had always meant graduated fever, terminated by bouts of illness. After securing a normal body temperature by rest, this patient was allowed a fair amount of exercise on alternate days, with such results that, after a few months, he was able to carry on daily a somewhat strenuous routine of garden work with only an occasional slight rise of temperature. For the first time in his career of many years of invalidism this man's symptoms and well-being have become amenable to command.

Several other somewhat similar cases could be cited with like results, so that for the past two years it has been my habit to require, as a routine when possible, rest on alternate days for all new patients, as well as for those who show morbid pathological instability, especially as regards temperature regulation. Such experiences should appeal to the clinical student of tuberculosis and the deductions from them should harmonize completely with experimental returns from the laboratory.

CLINICAL TUBERCULOSIS IN THE LIGHT OF EXPERIMENTS ON ANIMALS

It is a far cry from man to guinea pig, yet it may be asserted that this laboratory animal is a mine of knowledge to the clinician who would seek first-hand experimental information on the reactions of immunity.

The day is well passed when a clinician of intelligence would venture to contemn the teaching of laboratory experiments on the lower animals. Infinite as are the varieties of living matter there must be a familial chemical unity in all protoplasm, and just as certainly must the fundamental laws of vital reactions bridge the barriers of zoölogical classification.

It may not be out of place to interpose the observation that the practical clinician who ventures to deal with the data of developing research requires, far beyond the necessity of the purely laboratory worker, the faculty of wisdom. Speaking as of a court of law, he must combine in one the functions of counsel, judge and jury. For his is the sole responsibility of determining what newly developed facts illustrate the reactions of the human mechanism and what deductions may be therapeutically applied with all the probabilities in favor of salutary result.

Perhaps the most suggestive immunological reactions of the guinea pig can be elicited by instilling a liquid antigen into the nostrils of the animal. If horse serum to the amount of 0.2 cc. is dropped into the nose of a guinea pig there results a twofold sensitization to the horse serum. There is caused a general sensitization involving, no doubt, all the tissues of the body; but on this is imposed a special sensitization confined to the respiratory apparatus.

It may be said that to obtain a sufficient intensity of sensitization for demonstration purposes the nasal instillation of serum should be repeated three or four times, and that the special respiratory response is probably more constant in animals instilled after having been previously sensitized by subcutaneous injection of horse serum (4).

The respiratory response referred to is the production in the sensitized animal, within a few minutes of the instillation of serum, of an attack of bronchial asthma, curiously similar to the paroxysm as manifested in man.

Several facts establish themselves during such a series of observations on sensitized guinea pigs; the reactions, namely, depend (1) upon the size of the dose of serum which is administered by the nose; (2) upon the time interval elapsing between the successive doses; (3) upon the irritability of the animal's tissues at the time the instillation is given; (4) every dose of serum apparently affects tissue irritability and modifies its reaction to subsequent instillation; and (5) there is considerable individuality in the combination of these factors in different animals.

I will elaborate as briefly as possible these laboratory findings, always with the view of illustrating thereby the clinical phenomena of tuberculous toxemia. It must be borne in mind that my method of exhibiting the antigen was peculiar in that it involved no traumatism for the animal. The original purpose was to put in play as nearly as possible the procedures and mechanisms involved in the production of natural infection and natural immunity.

1. *The size of the dose of horse serum* instilled into the nose is of fundamental biologic importance. Using an amount of serum as large as 0.2 cc., the animal could usually be relied upon to become hypersensitive to serum, so that about fourteen days after four or more such instillations the animal would succumb with anaphylactic death on intravenous injection of 0.2 to 0.3 cc. of serum (5).

In my experience an animal once hypersensitive to this degree is always hypersensitive. I have made many and various attempts to render such creatures permanently nonsensitive but have always failed. Gay and Southard (6) themselves dwelt upon the fact that though an animal may for considerable periods apparently lose hypersensitiveness to a given protein, sooner or later its tissues swing back to the hypersensitive state. But it should be noted that, at least by the method of intranasal inoculation, it is apparently possible to establish complete immunity with little or no evidence of a preliminary stage of anaphylactic response to the antigen.

This is accomplished by instilling very small doses of serum, about 0.02 to 0.04 cc., into the nostril in tiny droplets. It has been found that a guinea pig treated in this way four to six times, on alternate days, when given intravenously a toxic injection of serum two weeks or more after the last instillation, is not usually disturbed (5). Reinjected after another interval of a fortnight the animal may manifest little or no anaphylactic response and the intravenous injections may be repeated with lengthening intervals and increasing dosage, up to more than 1 cc. (8).

Such an animal has been reinjected after a lapse of more than a hundred days with hardly perceptible reaction. It may be permitted to say here that the blood serum of such a guinea pig contains an immune body of unique character; for its transfer to the peritoneal cavity of a normal guinea pig seems able to confer on the animal something like *active* immunity to horse serum (7).

2. The resting interval between successive inoculations of antigen is important. In my work upon this subject, series of instillations were made with intervals varying from a few hours to twenty-four days (8). The field is one of extraordinary difficulty and conclusions deduced from numerous observations have little more weight than impressions. It appeared obvious that a single instillation of serum started immunological changes in the animal. Two instillations separated by intervals of one to sixteen days had a pronounced effect, but this modification of tissue chemistry gradually wore off. Four successive instillations, with intervals of forty-eight hours between, could produce apparently maximum resistance against a series of toxic intravenous injections. When instillations even so small as 0.02 cc. in amount were given daily, the establishment of resistance to toxic injections by the vein was much less marked. It is for these reasons that in tuberculosis therapeusis I have chosen resting periods of forty-eight hours as the optimum interval during which, on the average, the negative phase from one auto-inoculation due to exercise would pass over into the positive phase of increased resistance. It will be noted that we are detailing immunological data without the formulation of any theory of immunity.

3 and 4. The study seems to show that the exhibition of a certain amount of antigen may apparently have either of two opposite effects upon the sensitized animal. One is to increase and maintain the creature's hypersusceptibility, and the other is to increase its tolerance for the foreign proteins. The first effect is illustrated experimentally on the guinea pig when the serum dosages are separated only by intervals of twenty- four hours or less. Transferring our conceptions to the case of the actively tuberculous subject, auto-inoculations from muscular exercise when repeated at too short intervals may increase hypersensitiveness, while the same exertions spaced further apart may increase resistance. The student of tuberculosis can find in any clinic dealing in surgical infection, especially genitourinary infection, endless wealth of illustration for all the immunological phenomena of the pulmonary disease. Suffice it here to hold forth the fundamental therapeutic conclusion that a sure way to magnify an acute infection, to relight a subsiding one or transfer it to distant parts is through indulgence in ill-timed muscular exercise.

The other phase of antigenal reaction, the establishment of increased tolerance to the foreign protein, offers more difficulty in its analysis.

I may venture to mention a hypothesis that has grown out of the personal experiments that have been mentioned, namely, that resistance of an animal to the reinjection of a foreign protein may be due to two different states of molecular stability. It has been pointed out above that immunity of a guinea pig to the intravenous reinjection of a foreign serum can be acquired by preliminary spaced injections through a prolonged period. When the initial dosages of serum given by the nose are sufficiently small the first "toxic" injection by the vein may cause no disturbance, yet resistance to the repeated inoculation of similar doses shows that a certain immunity has been induced. An animal so treated has, after the lapse of nearly four months, withstood without disturbance the intravenous injection of one cc. of serum. Such a resistance may resemble what is called natural immunity; it would appear to be qualitatively different from that tolerance which may be acquired by an animal which, after a large initial dose of serum, becomes so "hypersensitive" that a second injection of the antigen after two weeks or more either kills or prostrates with a more or less intense anaphylactic shock. The nonlethal reinjection of serum in this case "desensitizes" the animal, so that for a limited period it may withstand the exhibition of an otherwise fatal dose of antigen. But such a resistance is usually brief, a matter of hours or days. It is a matter of great practical moment that the violence of reaction to the reinjected antigen is determined not only by the sensitiveness of the tissues but by the size of the dose. Reinjection with a sufficiently small quantity of serum temporarily desensitizes the animal, rendering it tolerant of otherwise lethal injections, without producing any signs of anaphylaxis.

Now the patient with clinical tuberculosis may be said to biologically resemble the animal made hypersensitive to a given foreign protein through a large initial injection. It would seem plausible that a promising therapeutic device for the amelioration of his disease might be offered by such auto-inoculations as would set up and prolong states of desensitization by intoxications below the threshold of anaphylactic sensibility. It is obvious, therefore, that an exact study of the phenomenon of desensitization in all its bearings is of fundamental importance to the establishment of scientific tuberculosis therapy.

As will be seen presently, Krause and his colleagues have experimentally investigated this subject and their results seem to point definitely to the conclusion that a state of anaphylactic shock distinctly lowers the resistance of an animal towards the organism whose product is used to produce anaphylaxis, but that anaphylaxis, *per se*, produced by a nonspecific foreign protein, as egg white, does not increase susceptibility to the propagation of experimental tuberculosis. Once again it seems worth while to revert to the suggestion made in a preceding section, that the immunity change produced in a hypersensitive animal by reinoculation of antigen is probably, at least, twofold; there is a "shock," lowering resistance; but there is simultaneously, and possibly qualitatively distinct, a "desensitization," raising resistance; undoubtedly the latter reaction can be isolated by lessening the quantity of antigen, and it would seem desirable to pursue observations along this line.

All this must be harmonized with the apparently irrefragable evidence that hypersensitiveness is the *sine qua non* of acquired resistance against infection, a conception which, as regards tuberculosis, has been admirably clarified in the teachings of A. K. Krause. In fact, the present discussion may well appear supererogatory to one familiar with this author's elaboration of the same subject (9), but its inclusion here seems necessary to unity of design.

Krause has given us valuable experimental observations on the effect of anaphylaxis on the susceptibility of animals to infection. He sensitized guinea pigs to tuberculo-protein and later induced nonlethal anaphylactic shock with the same protein (10).

During the shock the pigs were inoculated with a strain of living tubercle bacilli of low virulence. Also when the disease was established, he tested the effect on its course of inducing anaphylactic shock.

The first experiment gave only "suggestions that the extent of the disease was probably increased," though he had previously found that "resistance to infection is markedly lowered during the period that a sensitized animal is suffering from symptoms of anaphylactic shock (11)."

The second experiment showed that in an animal suffering from a low grade of tuberculosis "a single attack of anaphylaxis does not bring about conditions that favor the extension of the disease." Krause also found that the cutaneous hypersensitiveness to tuberculo-protein begins with the active general infection; "it varies directly with the extent and severity of the disease," and "it is diminished or completely wiped out during the period of a general tuberculin reaction" (an anaphylactic phenomenon) (12). In this connection, also, should be considered the interdependence of different infections as discussed by Krause and Willis (13). In the same paper these authors report the following important experiment: Guinea pigs were sensitized to egg white and later inoculated with tubercle bacilli of low virulence. The pigs were then divided into two lots. In one lot the animals were unmolested, but in the other they received large injections of egg white at intervals of 4 to 10 days. After the third injection of egg white the animals ceased to show anaphylactic response to it. The animals killed after 75 days led to the conclusion that "repeated protein intoxication, following upon infection with a comparatively avirulent tubercle bacillus, did not appreciably alter the animal's resistance to this microörganism." It does not, of course, follow from these results that repeated intoxications with *tuberculo-protein* would likewise prove negative to the course of an implanted tuberculosis.

Recently, also, Krause and Willis (14) took up the question as to the effect of local inflammation, *per se*, in promoting or opposing the fixation of tuberculous infection in the inflamed area. Failing to secure a satisfactory nonspecific inflammatory excitant, they infected guinea pigs with tuberculosis and injected intracutaneously these sensitized animals with tuberculin, some on the side of the original inoculation and some on the opposite side. Then, during various stages of the inflammatory tuberculin reaction they reinjected the animals with virulent tubercle bacilli in the reacting skin areas and compared the development of skin infection with that in animals treated in exactly the same way but without the injection of tuberculin. They concluded that if, because of an existing tuberculous infection, a guinea pig has acquired a certain degree of allergy and immunity, both of these are reduced under the following conditions: "1, They are reduced at the site of an inflammatory tuberculin reaction for at least four days after the application of the tuberculin. 2, They are more reduced by inflammatory tuberculin reactions at places which are within the lymphatic drainage area of tuberculous foci than at places which are not so situated. 3, They are reduced to a greater extent shortly (one to two days) after the application of tuberculin than later (four days after the tuberculin). The part played by the inflammation of the allergic reaction, considered purely by itself, remains undisclosed."

Very recently Auer (15) has developed conclusions bearing on this subject. He found that animals (rabbits) strongly sensitized with horse serum and then reinjected with the antigen undergo as a result a marked change in tissue reactivity towards nonspecific inflammatory irritants. Thus, "The skin irritant, xylol, when applied to the ears of sensitized and reinjected rabbits often causes a severe inflammation with the formation of crusts and destruction of tissue. Dry gangrene of the entire tip may result.

"The same agent, applied in the same dosage and in the same way, to the ears of (1) normal rabbits, (2) normal rabbits injected once with horse serum (serum controls), or (3) sensitized but not reinjected rabbits, causes only a mild inflammation with more or less edema. The inflammation and edema disappear in two or three days, leaving a practically normal ear." Auer considers the reaction in the reinjected animals as result of local anaphylaxis. "The inflamed tissues are more active metabolically than normal tissues and therefore the inflamed cells are affected by more antigen per unit of time than the normal cells. A subliminal concentration of antigen for noninflamed, sensitized cells may thus become effective when inflamed cells are concerned."

In a recent paper Watts (16) quotes Calmette to the effect that "if an animal is given a single small injection of tubercle bacilli, it would develop a marked immunity; but if it were given a number of small injections at frequent intervals, it died more quickly than the unprotected animal, showing that reinfection in the period of sensitization immediately after primary infection is a peculiarly deadly thing." Watts unfortunately hazards the statement that sensitization is a phenomenon which is lost soon after primary infection.

It is not necessary to understand the full significance of all these laboratory experiments to apprehend that their moving forces are the same that determine the course and reactions of clinical tuberculosis. We know absolutely that the tuberculous individual is in a class by himself in his reactivity to tuberculin intoxication. We confidently believe that inoculation of such a person with tuberculo-protein initiates at once a biologic response, having two opposite possibilities for the welfare of the individual: one is disease, the other is health. Viewed broadly, such a union of opposed variables is not a function of pathological states alone but is intrinsic in all physiological and psychological reactions; but this theme must now rest with the mere suggestion.

Sir Almroth Wright has given a most useful graphic conception of the biologic response to infection in portraying it as a wave which descends below the base line in a "negative phase" to represent the lowering of tissue defense following inoculation with an antigen but which normally takes its course upwards into a "positive phase" of increased resistance, which could not have been realized except as a rebound from the former depression. This graphic conception seems to me to illustrate vividly the actual necessities of tuberculosis practice: the interval separating his successive auto-inoculations is of supreme importance to the welfare of the patient. An antigen introduced during persistence of the negative phase will only send this to a greater depth, but reserved till the positive phase is near its crest will tend to raise this to a higher maximum.

It is this conception, growing out of actual clinical experiences, that has given occasion for this paper. Paterson put it to a practical test more than ten years ago, but no one can pretend that even to-day it is generally entertained.

5. Finally, nothing is clearer in animal experimentation than that different individuals may vary greatly in their response to environmental change, in the violence of their response, for example, to injections of foreign proteins. This fact becomes of the highest practical importance in study of the human kind.

SUMMARY AND CONCLUSIONS

1. Based on the common experience that clinical deterioration due to tuberculous disease is not only accompanied but is preceded by more or less well-recognized pathological symptoms, it is maintained that on investigation each patient will commonly disclose a range of pathologic symptoms far less obtrusive than those usually apparent to the physician and the recognition of these may lead much earlier than is usual to proper treatment.

2. Based on the fact that auto-inoculations in the tuberculous subject may lead to disaster or to cure, depending on the phase of vital reaction at which each inoculation succeeds the preceding, it is shown by clinical experience and made reasonable by experimental inquiry that the clinician should take careful account of the length of the rest interval between muscular exertions of certain patients. It has been found that patients whose symptoms persist when even gentle exercise is taken daily may overcome this trouble when exercise is spaced on alternate days. There is probably considerable divergence between the length of the "negative" and of "positive" phases of reaction in different persons and accordingly the spacing of their exercise should differ.

3. An attempt has been made to draw a parallel between the obscure events marking the course of clinical tuberculosis and the immunological

reactions of animals in which the conditions of infection and inoculation can be experimentally controlled.

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ADDITIONAL DIAGNOSTIC METHODS FOR CASES OF SUSPECTED INTRAOCULAR TUBERCULOSIS[1]

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The routine type of investigation which I would suggest for these cases suspected of being tuberculous etiologically will, I believe, appeal to you as a logical method of observation and refinement in diagnosis, if I may devote a few moments to certain general considerations of tuberculosis regarded differentially as an infection and as a disease.

The significance of new data, even though accepted by the profession, often fails to affect our real attitude; and we are likely to regard such information as academic in value, if it seems to have no practical bearing on our cases. This is particularly true regarding the accepted evidence which postmortems have supplied us with reference to the high percentage of anatomical tuberculosis and the large proportion of both children and adults who will give positive tuberculin reactions. As a direct outgrowth of these two lines of investigation, the terms tuberculous infection and tuberculous disease were introduced as expressive of our changed conceptions regarding tuberculosis. On these grounds, if we can demonstrate an anatomical lesion, or postulate one on the basis of a positive tuberculin reaction but believe that there are no symptoms referable to this possible lesion, we call the condition tuberculous infection[2] and imply thereby that the bacilli are dead or nonactive, or the lesion is fibrosed and for the moment effectually cut off from the rest of the body. The term tuberculous disease we reserve for those cases in which we believe the pathlogical lesion to be active and consequently in part or wholly responsible for the symptoms. Our usual methods of examination—clinical, X-ray, and the tuberculin test—are not sufficient to allow us to use these terms in the diagnosis of our cases with any degree of certainty: indeed their frequent use presents pitfalls and incline us to errors in diagnosis. If we desire to apply this conception in the practical diagnosis of clinical tuberculosis and detect those clinical lesions at a time when they might be described as close to the border line of the nonclinical infection we must devise additional means of obtaining information.

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[1] Read before the Section of Ophthalmology and Otolaryngology of the Academy of Medicine, Toronto, December 13, 1920.

[2] The application of the term, *infection* in this sense is that condition *continuing from the subsidence of the disease which is assumed to be coincident with the production of the lesion,* microscopic or gross, by the original implantation of bacilli. *It is not the mere usual meaning of being coincident with implantation and take of the bacilli..*

Comparatively recently the British Government[3] has published one of its most valuable investigations which had to do with tuberculous lesions found postmortem and the correlated results regarding the presence or absence of living bacilli.

TABLE 1

To indicate probable state of tuberculous infection; as correlated with postmortem anatomic and bacteriological findings in 195 deaths from all causes between 2 and 10 years

	PER CENT	DISEASE HAD MADE*
Total incidence of tuberculosis	60.5	
(1) Anatomic lesion + tubercle bacilli apparently dead	10.3	Progress followed by retrogression
(2) Anatomic lesion + tubercle bacilli cultured	47.2	Essentially progress, with variations in retrogression
(3) Anatomic lesion 0 tubercle bacilli cultured	3.1	Unknown progress or retrogression (a) Threshold of early progress (b) Threshold of early retrogression

* Remarks under this column have been added to the percentages taken from the table in Report 88.

Table 1, taken in part from this publication, is of special value in that it gives a bird's eye view, so to speak, of the rôle which tuberculosis was playing in children whose death from all causes occurred in hospitals not specially devoted to the care of tuberculosis. The correlated bacteriological findings give us proof that even within the first decade of life both minimal and gross lesions may be found with and without living bacilli, and that within this time tuberculous disease may be altered to that arrested stage which may be regarded as the threshold of tuberculous infection, which state in turn we must regard as practically the normal condition of the majority of adults remaining free from clinical tuberculosis. In another way it supports the findings obtained in children by the use of the tuberculin test, and the conception that a positive tuberculin sensitiveness (or test) can only be caused by a definite implantation with living bacilli resulting in microscopic or gross lesion.

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[3] Report 88, new series, 1914: (1) The incidence and bacteriological characteristics of tuberculous infection in children. Eastwood and Griffith. (2) An enquiry based upon a series of autopsies into the occurrence and distribution of tuberculous infection in children, etc. A. S. Griffith. Published by Darling & Son, 1914.

The particular percentage among these cases in which either death, apparent arrest or complete recovery might have taken place is immaterial: that "apparent arrest" can be demonstrated in a percentage of cases during these early years is the important feature.

This table and the published details of the investigation pleased me in particular because, since about 1910, I have steadily attempted to record and repeat certain biological tests not only on the positive and suspected tuberculous, but upon the intimately exposed and the clinically normal as well, in the hope that chance might demonstrate the value of changes in the biological results thus obtained by some definite correlated clinical manifestation.

Incidentally, the D. S. C. R. chest clinic afforded for the first time an opportunity in which it seemed possible to approach the conditions which one must regard as the necessary and accessory controls to this biological or immunological aspect.

While it would not have been possible to clinically examine these particular children before death with respect to differentiation between tuberculous disease and infection, because they were ill in varying degrees from all causes, yet the correlated pathological and bacteriological results given in the table serve to demonstrate, I think, the uselessness of such an attempt. Yet methods which would allow us to obtain an approximately accurate classification between tuberculous disease and infection upon these children, for instance, are undoubtedly necessary, if such methods are to be of value in an important proportion of the cases suspected of intraocular tuberculosis.

Primarily, as an indication of the possible tuberculous etiology of any eye condition, as I conceive it, it will be necessary to differentially diagnose between tuberculous infection and tuberculous disease elsewhere within the body. Secondarily, it will be necessary to detect evidences of those minimal lesions which are often called sluggish, subacute, or low grade, but which to me mean that the margin between host-resistance and virulence of infection is very narrow, though probably this margin is rarely a constant for long. Granted that definite tuberculous disease is demonstrated elsewhere in the body, positive evidence is thus afforded the oculist that the suspected intraocular lesion can be tuberculous, but the final decision, based upon this data plus his own focal observations, must rest with the oculist.

Before dealing specifically with your problems of diagnosis let me return to the general subject of tuberculosis and attempt a speculative analysis of these groups of cases with particular reference to the possibility of arrest of lesion. Or, otherwise expressed, how might one have expected these cases in their different groups to have reacted to their tuberculosis, had they not died from other causes?

In group 1, inasmuch as living bacilli could not be demonstrated in many of the gross lesions—in some cases all the gross lesions and elsewhere as well—one can only conclude that the host had got rid of most, if not all, of the bacilli, even after they had succeeded in multiplying and in producing lesions. Although reinfection clinically might have occurred in some at a later period, complete recoveries would have been accomplished in a percentage of the cases. The clinical diagnosis of these lesions would have been dependent to a considerable extent upon their size and location, but the differentiation could rarely, if ever, have been made between tuberculous disease and infection: it isn't always possible to do this at the postmortem.

In group 2 death was or would have been caused by the clinical tuberculosis apparently in the great majority of cases.

In group 3, the most interesting of all, it is of course impossible to predict the result. The findings can be interpreted as representing a progressing recovery from a microscopic lesion or as representing an initial lesion which would have increased and later be found either in group 1 or 2.

From this attempted analysis it is apparent that, in the majority of cases which would have presented difficulties clinically, the differential diagnosis between disease and infection is *chiefly, if not wholly, dependent upon the prognosis*. That the terminations or clinical outcome which I have suggested for each group are undoubtedly possible cannot be denied. Group 1, the group of apparently arrested lesions (and this within the first decade of life), supports this; the evidence of healed tuberculous lesions found postmortem in adults and, further, the clinical evidence which we have every day of complete recoveries from extensive pulmonary lesions force one to admit this.

Thus far I have taken a good deal of time to state in a roundabout fashion that the result, once the B. tuberculosis has entered the tissues, is dependent upon the outcome of host resistance versus virulence of infection. May I, however, emphasize this by stating that, following the implantation (meaning thereby introduction within the tissues from any of the routes of infection) of bacilli we always have tuberculous disease, that only through the lapse of time and because of the host's resistance can this be converted into tuberculous infection. There is seemingly no reason why we should not assume that infection thus defined may not be evolved from the microscopic as well as the gross lesion.

When the lesion is gross in character, our usual methods may allow us to detect it. It may be, however, that the present and past medical history in a few such cases will leave one in some doubt as to the possibility of activity on the part of the lesion. In acknowledging such a contingency one expresses the need of data relative to the hypothetical immunological processes which take place within the host while tubercle bacilli remain alive or multiply within the lesions they have occasioned. As I have previously mentioned, the etiological character of a local lesion (such as an intraocular) is not *necessarily* tuberculous because tuberculous disease can be demonstrated elsewhere within the body. The more concise, however, the information regarding the likelihood of such a lesion acting as the parent focus, the greater its diagnostic value to the oculist.

When however, after implantation, tuberculous disease persists as a comparatively slight lesion and in some state closely allied to that from which true tuberculous infection is evolved, there is always the possibility for the development of foci elsewhere in the body and the difficulties of diagnosis must always be great. It would appear to me that it is in these cases that intraocular lesions, atypical in appearance, will occur and their etiology be determined only by careful investigation.

When cases are patently tuberculous in the clinical sense there is no need for refinements in diagnosis and such can be excluded from the discussion to-night. The remaining cases can perhaps for ease of presentation be divided as already suggested, into two classes:

1. Those in which it is possible to demonstrate a definite anatomical lesion. Our problem here is to determine whether this lesion is "dead,"

that is, is it, and has it been completely walled off, or, failing that, are the bacilli dead? In such circumstances it cannot have acted as a parent focus. If the bacilli are not dead and some have been transplanted elsewhere in the body, the resistance or tolerance of the host must be high, or otherwise the foci would be active and the amount of involvement increasing.

2. Those cases in which it is not possible to demonstrate a definite pathological lesion, but in which we suspect a more or less minimal involvement. Presupposing such a lesion, we must conclude that the resistance of the host is high again because of the absence of increasing involvement.

Thus our problems apparently always centre about this immunological aspect of resistance. For their solution we need methods of demonstrating an etiological relationship between the host and the B. tuberculosis, with regard to the differentiation between tuberculous disease and infection, and which must at the same time give some indication regarding the specific resultant of host-resistance versus infection-virulence; or, otherwise expressed, the diagnosis is contingent upon the prognosis.

The methods which we have now will, I believe, be found to be helpful in this regard; and this type of etiological relationship can best be demonstrated by the simultaneous use of three tests, namely, the inhibitive reaction, the complement fixation reaction, and the quantitative tuberculin test.

The various end reactions which these tests give under different conditions (immunological or pathological) may be summarized as follows:

1. The inhibitive reaction has four end results looked at from the laboratory point of view. Clinically we can group these as (1) a slight reaction and (2) a marked reaction.

The slight reaction is found in most normal adults, and in those cases (clinically tuberculous) whose progress is at the moment distinctly unfavorable.

The marked reaction, among the positively (clinical) tuberculous, is found only in those cases which are apparently doing well or whose work tolerance is comparatively high. It has frequently been found in those for whom at the time it has not been possible to demonstrate a definite lesion, although there have been grounds for clinically suspecting tuberculosis in varying degrees, and it has rarely been found in apparently normal individuals. If it were not found in these latter two questionable groups, I would long ago have had grave doubts regarding its specific value.

To what extent my present conception regarding tuberculosis is due to the results of this test in conjunction with the other two methods mentioned, or other experimental data, or general clinical experience, it is difficult for me to estimate. For approximately the first 500 cases this reaction was the chief feature with which I tried to correlate other data. Since the war especially, I have had it available merely as a means of additional information on well over 2000 cases, and used in the manner suggested by these remarks.

One does not attempt to bring forward any immunological reaction as even approximately indicative of specific resistance to the B. tuberculosis without a great deal of misgiving. From the experimental point of view such an interpretation must remain very questionable until the reaction can be produced experimentally, and in this way one can obtain and regulate the necessary controls. From the clinical point of view merely the realization of the uncertainty of attempting to interpret in the human subject any apparent change in the symptom complex, any change in the well-being, etc., as evidence of progress or retrogression of the tuberculous lesion, would of itself cause one to hesitate long before accepting such correlation between a laboratory reaction and clinical progress.

The different types of onset and course met with in tuberculosis, including the variations normally incidental to the disease as a glandular, as a pulmonary, as an epithelial, or as a serous membrane infection demonstrate that, for each of these anatomical types, other factors which may have little or no relation to specific resistance are also concerned in the development of the tuberculous lesions. As a possibly accidental and certainly mechanical factor, the character of the lymphatic system, as demonstrated by Krause (1) undoubtedly plays a most important rôle in the arrest of bacilli and localization of lesion. In the development of the lesion Foot (2) has shown the important part which the endothelial cells play: they migrate to the focus and in proportion to this attraction they multiply *in situ* and may thus interfere with the local blood supply. Necrosis and caseation are in turn influenced by this change in the vascular system. These endothelial responses are certainly biological in character, but possibly they are only indirectly related to specific resistance.

Despite this type of data and its undoubted relation to the development of clinical tuberculosis, the dominant factor is still specific resistance, and all my evidence goes to show that the marked inhibitive reaction is specifically bound up with, or accidental to, a grade of resistance on the part of the host which is evidenced clinically by a comparatively nonprogressive type of the disease. Expressed as a hypothesis it would seem that following implantation of the bacilli a marked inhibitive reaction will be obtained if the specific resistance of the host in contrast to the virulence of the infecting bacilli is high. That this margin of comparative safety may vary during even a subacute type of the disease would seem to be the explanation of the comparatively rapid changes in the reaction which will occasionally be found under varying circumstances. Clinically this is undoubtedly what one expects and finds. Again, in cases which have been followed from definite (or inferred) clinical tuberculosis to apparent arrest or better, the marked reaction is comparatively rapidly replaced by the slight reaction, so that one can state that the marked reaction is seemingly obtained only in clinical tuberculosis, which at the time is one of favorable prognosis. These will include those cases in which the lesion can be demonstrated, and also those in which the presence of the lesion is inferred and can only be regarded as a matter of individual opinion.

The possibility of technical errors incident to the performance of the test in the laboratory is such that I would place the percentage of experimental error for the inhibitive reaction as higher than that obtained with the complement fixation reaction.

2. The complement fixation reaction from the laboratory point of view is obtained in varying degrees of positiveness from a doubtful to a strongly positive (or four plus) reaction.

Clinically it may be positive at any time during or subsequent to the active duration of the disease. Among the definitely tuberculous there is a slight preponderance of unfavorable cases giving a positive result, in particular those giving the strong or four plus end reactions. This characteristic would, I think, be much more apparent if we excluded those cases in which it is not possible to demonstrate a lesion, as well as those cases which on other grounds one would classify clinically as "quiescent," "apparently arrested," or "arrested," etc. Regarding these two latter groups, the "lesionless" and the "arrested," there is this to remark, that frequently with the disappearance of the marked inhibitive reaction a positive complement fixation appears and persists for a long time. Cases with and without a definite anatomical lesion have been followed in which this sequence of biological reactions has been noted.

It is probably this fact—the persistence of a positive complement fixation after the detectable activity of the tuberculous lesion has apparently subsided—which has prevented this test from being regarded as a reliable aid in the diagnosis of clinical tuberculosis. Yet it is this particular characteristic of the test which, when combined with the inhibitive reaction, so enhances its value. Thus in an "apparently arrested" case, with demonstrable anatomical lesion, the appearance of a positive complement fixation reaction (this test previously being negative) has repeatedly been found to correspond chronologically with the disappearance of clinical evidences of activity (or the disease per se) and with the continuance of favorable progress. So in cases in which no anatomical lesion could be demonstrated the appearance of this reaction may be regarded as of similar diagnostic value to the positive tuberculin test in infancy and early childhood; or, otherwise expressed, as an evidence that the B. tuberculosis has produced comparatively recently at least a minimal lesion which—while the activities implied by the term lesion lasted—was true tuberculous disease. As such, the condition would be clinical tuberculosis except that the diagnosis could not be made because of the lack of sufficient evidence.

In these cases—the "arrested" and the "lesionless"—the complement fixation reaction is frequently of but slight or doubtful degree. Such results would necessarily have to be regarded as possibly due to technical error, especially if obtained initially; but, where the case had previously been fully investigated, such end reactions can be regarded as true because of the chronological sequence of both reactions in correspondence with the clinical course.

Relative to experimental error this feature is to be noted; that in the same serum the nonspecific serological factors favoring a positive complement fixation reaction are such that they tend to prevent the marked reaction being obtained with the inhibitive technique. Thus the possibility that a technical error is responsible for both a doubtful complement fixation reaction and a marked inhibitive reaction in the same serum is almost nil.

Correlated with the frequent persistence of a complement fixation in a supposed clinically arrested case is the fact that a positive complement fixation reaction is readily produced in animals by the injection of simple extracts of the B. tuberculosis. It is not necessary either to induce a tuberculous lesion or inject living or even whole bacilli.

The possibility of experimental or technical error incidental to the performance of the tuberculocomplement fixation test may be approximately represented by stating that it bears to the Wassermann reaction the same increased percentage of technical error which the inhibitive reaction bears to it. In other words the reliability, from the purely technical point of view and with regard to the separate serological factors concerned, of the end results obtained in the laboratory with these three tests is in the following order—the Wassermann reaction, the tuberculocomplement fixation reaction, and the inhibitive reaction.

3. As regards the tuberculin test, my own preference is distinctly in favor of the intracutaneous test which I use quantitatively, carefully record, and repeat after an interval of from three to six weeks or longer. The purpose of this repetition is merely to demonstrate whether or not any change in the degree of sensitiveness has taken place within the period of time elapsed. Theoretically, I have felt that any marked change in sensitiveness could only be obtained in cases which were clinically tuberculous. The results can hardly be regarded as absolute, but any marked variation in sensitiveness would to me be very suggestive of tuberculous disease in contrast to infection.

The use of the phrase, positive tuberculin test, is merely a convenient method of stating that there is evidence of positive specific sensitiveness, the exact degree of which is not expressed. As this range of sensitiveness may vary many thousandfold, and as in its lowest degrees its presence may be questionable, it is important that the result should not be merely noted as positive or negative, but that the degree of sensitiveness should be recorded. In the interpretation of the physical signs obtained by clinical examination of a patient we rely in varying degrees upon the past medical history; so in like manner the interpretation of the biological data obtained to-day would undoubtedly be of more definite clinical significance were the results of these reactions performed previously available for comparison.

I have adopted this method of using the tuberculin test because, in my opinion, the result of a single test is practically valueless from the standpoint of diagnosis. I believe this chiefly because (1) a proved negative result will not exclude clinical tuberculosis, as has been shown by positive cases doing well and making an "apparent arrest;" nor (2) is a marked degree of sensitiveness necessarily indicative of clinical tuberculosis, or necessarily recent tuberculous disease in contrast to tuberculous infection.

These remarks are of course to be modified for early childhood. They are to be modified for this age because a positive tuberculin reaction in adults of itself indicates only that tubercle bacilli have in the past been implanted within the host, and that the host has reacted. It does not give any indication of the outcome subsequent to the initial reaction. But, if this implantation and reaction can have taken place only within a few years, as in childhood, it naturally acquires greater significance than in the adult.

The general and focal reaction I should think would be of considerable diagnostic value in intraocular tuberculous disease. I have not however found it so in pulmonary lesions. A focal reaction will be produced only in the presence of a general reaction, and for this reason there are certain natural objections to it. If its use is decided upon, the degree

TABLE 2

Relations between the several reactions and underlying etiological and clinical factors

	CAUSATIVE, PATHOLOGICAL OR IMMUNOLOGICAL LESION	CONDITIONS GOVERNING APPEARANCE AND DISAPPEARANCE
Positive tuberculin sensitiveness	A. Positive tuberculous lesion (accepted)	Maintained indefinitely (many years) In tuberculous disease, indefinitely (with rare exceptions) In tuberculous infection,* indefinitely (with rare exceptions)
Positive tuberculo-complement fixation reaction	A. Positive tuberculous lesion (accepted) B. Injection of extracts of bacillus tuberculosis (proved) C. Absorption of by products of tuberculous lesion in which bacilli are dead (assumed)	A. Temporary or persistent throughout course of disease (in approximately 50 to 70 per cent of cases) B. May first appear or persist during development of infection
Marked inhibitive reaction	A. Positive tuberculous lesion (assumed)	A. During course of disease when work tolerance (or resistance) is comparatively high B. Disappears at onset of a severe flare up C. Disappears at threshold of infection

* The term infection has the same application as defined in the body of the paper.

of tuberculin sensitiveness, as ascertained by one of the cutaneous methods, will give one an approximately accurate clue to the amount which will be required to produce the general and consequently the focal reaction. At any rate, in this way one is not likely to induce an excessive and unnecessary general reaction with the dangers that might accompany this.

In table 2 I have attempted to graphically represent the circumstances under which these reactions may be produced etiologically and the subsequent clinical conditions under which they may disappear or persist.

A recapitulation of what I have tried to present as additional diagnostic methods for cases of suspected intraocular tuberculosis might be put as follows:

A. *With regard to the methods themselves:*

1. A careful clinical and, frequently, a stereoscopic examination.

2. The simultaneous use of the three tests, namely, the inhibitive reaction, the tuberculocomplement fixation reaction, and the estimation of the degree of tuberculin sensitiveness.

3. The repetition of these tests, and if the diagnosis still remains in doubt the additional use of the general and focal reaction to tuberculin.

B. *With regard to the interpretation:*

1. The presence of a marked inhibitive reaction together with slight or even doubtful complement fixation is in my opinion an absolute indication that the patient has an active tuberculous lesion, as well as a comparatively high work or resistance tolerance.

2. With a marked inhibitive reaction alone I would hesitate to place upon it the same amount of reliance, chiefly because of the greater possibility of the technical error. Here of course the degree of the end reaction is of importance.

3. With a positive complement fixation reaction alone the degree of the reaction is of importance. A strongly positive result almost excludes the possibility of technical error and is of corresponding diagnostic value, but it is comparatively rare that this degree of reaction will be found in cases in which there would be any clinical doubt regarding the diagnosis. The slight and even doubtful reactions, when true results, have frequently the clinical value in adults which we give to a positive tuberculin test obtained in very early childhood, and as such they must be considered as part of the clinical *precis*. At the same time

however, the greater possibility of technical error must be considered in these mild and especially the doubtful reactions.

4. In the event of certain of the "indecisive" results indicated in 2 and 3, the tests should be repeated, and if the reactions are unchanged they should be considered as suggestive only and taken together with the clinical data and with the history of the subsequent course of the case.

5. Any marked variation in the degree of tuberculin sensitiveness should be considered as suggestive of tuberculous disease rather than of infection.

6. If the repetition of these tests gives the same "negative" results, namely, a slight inhibitive reaction and a negative complement fixation reaction, the data should be regarded as of increasingly exclusive value in proportion to the number of such results, and the length of the period of observation.

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THE ADRENALS AND THYROID IN EXPERIMENTAL TUBERCULOSIS

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Last year, in connection with some experiments on tuberculosis in guinea pigs which had had one adrenal removed, we reported an increase in the weight of the adrenals in animals with generalized tuberculosis, as compared with nontuberculous animals, occurring both in the hypernephrectomized pigs and the controls (1) (2). We added, "This suggests a demand for increased adrenal function in tuberculosis, and calls for further experiment with a larger number of pigs and a more complete record of body weights."

During the last eight months we have kept a record of the adrenal weights and body weights of numerous unselected tuberculous and nontuberculous guinea pigs. We have analyzed these figures at intervals, and the results have been so constant that it seems unnecessary to wait longer before reporting the confirmation of our former inference. The results are given in tables 1 and 2.

These figures make the following facts very clear:

1. That there is an increase in the absolute and relative weights of the adrenals in the progress of tuberculous disease in these animals, and that this is real, not apparent, that is, it does not depend on changes in body weight.
2. That a similar enlargement occurs in other infections (pyogenic abscesses and septicemia).

The left adrenal averages somewhat heavier than the right, but it did not seem desirable to complicate the tables with these unimportant data.

We have not found any specific changes in the microscopic picture of the enlarged adrenals. There is perhaps a slight hyperemia, but this is hard to prove in an organ normally so vascular. The medullary tissue does not seem to be increased; if there is true hyperplasia, rather than the mere cellular hypertrophy and increased blood supply of active function, this hyperplasia is probably cortical. Cortical hyperplasia

TABLE 1

Summary of experimental data

GROUP	NUMBER OF GUINEA PIGS	AVERAGE BODY WEIGHT	AVERAGE WEIGHT OF BOTH ADRENALS	AVERAGE WEIGHT OF BOTH ADRENALS EXPRESSED IN PER CENT OF BODY WEIGHT	PER CENT INCREASE OVER NORMAL
		grams	*grams*	*per cent*	*per cent*
Nontuberculous, all	34	583	0.412	0.071	9
Nontuberculous, with pyogenic infections	8	581	0.487	0.084	29
Nontuberculous, emaciated, no pyogenic infection	1	375	0.4	0.107	65
Normal	25	592	0.388	0.065	
Tuberculous, all	23	584	0.463	0.079	22
Tuberculous, emaciated	3	362	0.483	0.133	105
Tuberculous, not emaciated	20	618	0.46	0.074	14
Tuberculous, not emaciated, killed less than 6 (average 4) weeks after inoculation	8	595	0.4	0.067	3
Tuberculous, not emaciated, killed 6 to 15 (average 10) weeks after inoculation	12	633	0.5	0.079	22

TABLE 2

Comparison of tuberculous and corresponding nontuberculous groups

GROUP	NUMBER OF GUINEA PIGS	AVERAGE BODY WEIGHT	AVERAGE WEIGHT OF BOTH ADRENALS	AVERAGE WEIGHT OF BOTH ADRENALS EXPRESSED IN PER CENT OF BODY WEIGHT	RELATION OF PER CENT ADRENAL WEIGHTS IN TUBERCULOUS GROUP TO PER CENT ADRENAL WEIGHT IN CORRESPONDING NONTUBERCULOUS GROUP
		grams	*grams*	*per cent*	*per cent*
Nontuberculous, all	34	583	0.412	0.071	
Tuberculous, all	23	584	0.463	0.079	111
Normal	25	592	0.388	0.065	
Tuberculous, not emaciated	20	618	0.46	0.074	114
Nontuberculous, emaciated, no pyogenic infection	1	375	0.4	0.107	
Tuberculous, emaciated	3	362	0.483	0.133	124
Nontuberculous, with pyogenic infections	8	581	0.487	0.084	
Tuberculous, all	23	584	0.463	0.079	94

has been reported by Stilling, and confirmed by Crowe and Wislocki (3), in the compensatory hyperplasia which follows removal of one adrenal, or part of one. Similar cortical hyperplasia has been reported by Biedl as occurring in pregnancy. Calmette (4) mentions enlargement and congestion of the adrenals as a feature of fatal poisoning in tuberculous guinea pigs.

In only one instance have we found tuberculous lesions in the adrenals. This was in a case of overwhelming general tuberculosis with emaciation, following intraperitoneal inoculation. The lesions were in the medulla.

We have no direct evidence bearing on the behavior of the adrenals in human tuberculosis. We have already referred in our former paper to the observations of Sergent (5) on the beneficial effects of adrenalin in asthenic tuberculous patients, and we have verified this in our own clinical experience. Crowe and Wislocki point out that since it is the cortex which enlarges to meet an adrenal insufficiency, and since the cortical tissue is limited to the adrenals, while the chromaffin tissue of the medulla occurs elsewhere as well, it would be more reasonable in "cases of acute and chronic infection with symptoms suggesting adrenal insufficiency," to give an extract derived from the cortex, instead of adrenalin, which is derived from the medulla. They noted focal necroses in the cortex of a dog with reduced adrenal tissue and a chronic infection, and make the suggestion in consequence of this observation. Their experiments lead them to believe that there is some sort of interrelation, not only between the adrenals and the other endocrine glands, but also between the adrenals and the lymphoid tissue.

All study of the endocrine glands emphasizes their coördination as parts of a system of autotherapeutics which we crudely endeavor to imitate and reinforce with our stimulants and sedatives. This fact leads us to refer briefly to some former observations on the thyroid in tuberculosis. In 1915 two of us (Webb and Gilbert) carried out some experiments on this subject. These were outlined in a general discussion of immunity in tuberculosis (6), from which we may quote here:

> A small number of experiments were undertaken to study the effect of the removal of the thyroids upon tuberculosis in guinea pigs. Portions of the thyroid gland varying from three-fourths to the whole amount were removed under ether. Under similar conditions, the thyroids of the control pigs were

exposed but not removed. Four weeks later each pig received in the nipple area a subcutaneous inoculation of forty living virulent human tubercle bacilli. The general results may be briefly summarized as follows:

Series A. Three-quarters of the thyroid tissue was removed:

1. The general appearance and condition when killed was strikingly different. While the control pigs were thin and emaciated and dying, the others were fat and healthy in appearance.
2. The amount of tuberculosis produced did not differ materially in the two sets of pigs.
3. Local lesions were more frequent and prominent in the controls.
4. Hyperemia of the remains of thyroid tissue was noted at autopsy.

Series B and C. All thyroid tissue was removed:

1. The extent and distribution of the tuberculosis were not affected.
2. The pigs without thyroids showed marked signs of myxedema.

In general, tuberculous guinea pigs which have been killed during the course of the disease have shown enlargement of the thyroid gland.

The influence on the course of established tuberculosis was also studied. The tuberculous pigs from whom the thyroids were removed died earlier and had more extensive tuberculosis than the controls.

These experiments would seem to suggest that in tuberculous infection in guinea pigs the thyroid gland tends to hypertrophy but that any decided bearing on immunity processes is not detected.

As regards the thyroid, clinical observations are somewhat more satisfactory than in the case of the adrenals. Nearly twenty years ago Turban (7) wrote, "A concomitant of the first stage of tuberculosis of the lung is a slight swelling of the thyroid gland, which I have noticed in a fifth of my cases in the first stage; more rarely later in the disease." Stanton (8) in 1905 referred to this early enlargement, with symptoms suggesting hyperthyroidism.

In connection with the report of our experiments, the following statement was made, "An enlargement of the thyroid gland is very frequent in early stages of pulmonary tuberculosis, whereas in late stages of the disease this gland would appear to share in the general atrophy. When enlarged, it is generally soft to the touch."

In 1917 Strouse (9) stated that signs of hyperthyroidism are common in early stages of pulmonary tuberculosis, but disappear as the lungs clear up. Recently, Courland (10) has reported hyperplastic changes in the thyroid in acute tuberculosis, hyperplastic and sclerotic changes in chronic tuberculosis, and sclerosis in cured tuberculosis. He seems inclined to attribute a tuberculous tendency to persons with hyperthyroidism (11).

It seems more probable to us that this increase in the size and function of the thyroid is a phase in the marshalling of the body's defensive forces against the invading disease. At the Mayo Clinic, where vast numbers of cases of exophthalmic goitre are treated, it has been observed that tuberculosis is much rarer in persons with this disease than in the general population (12). Thyroid extract, as well as adrenalin, or an extract of whole adrenal, or of adrenal cortex, might well be beneficial to some of our tuberculous patients, and it seems desirable to give this accessory to the treatment of tuberculosis a trial, beginning with minute doses.

CONCLUSIONS

1. The adrenals become enlarged in guinea pigs in the course of generalized tuberculosis, and also in pyogenic infections.
2. The thyroid gland also appears to enlarge in experimental tuberculosis of guinea pigs, as well as in certain forms of human tuberculosis.
3. This enlargement of adrenals and thyroid is probably in response to a demand for increased function, and it may be desirable to supplement this tendency by giving adrenal and thyroid extracts in selected cases of human tuberculosis.

This study has been made possible through the generosity of Mrs. B. C. Allen of Colorado Springs.

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PRESIDENTIAL ADDRESS

TUBERCULOSIS; THE RATIONALE OF RESEARCH

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We look on nature with our eyes, not with our reason.
Truth lies deep, and must be fetched up at leisure.—SENECA.

To-day gives me the first opportunity to thank you for the great honor you conferred last year in making me President of The National Tuberculosis Association. The gift is the highest that can be received by one working in this field, and after twenty-five years of work in tuberculosis, gratitude, "the fairest blossom which springs from the soul," is your due.

The great world calamity through which we have passed, so far in safety, has led many to inquire where civilization now stands, and what is its future. Tuberculosis also, a concomitant of civilization, may well be reviewed in similar fashion at this time. We must frankly state our knowledge of the disease, and also the extent of our ignorance regarding tuberculosis, so that we can more wisely guide the efforts made in prevention and cure, and direct research to bring further enlightenment.

THE PRESENT STATE OF OUR KNOWLEDGE

Confucius said, "When you know a thing, to hold that you know it; and when you do not know a thing, to allow that you do not know it; this is knowledge."[1] Let us briefly analyze our knowledge of tuberculosis in the spirit of this definition, considering first the things we know, then the things we do not know.

We know:

1. That tuberculosis is infectious, in origin parasitic.
2. That it is caused by a specific microörganism, the tubercle bacillus.
3. That certain more or less characteristic tissue changes in the victim occur in its course.
4. That the conflict between bacillus and host often ends very early in favor of the host—so early that the presence of the disease is not suspected during life.

5. That in the majority of the cases which are recognized clinically, the disease shortens life.

6. That its morbidity and mortality rates are still high throughout the civilized world.

7. That there are symptoms and signs, some or all of which are present in recognized cases.

8. That exhaustion and malnutrition in the host contribute to the development of the disease, while rest and adequate feeding favor resistance.

9. That of all the countless remedies proposed, REST alone has stood the test of time.

10. That a tuberculin reaction indicates at least infection and invasion by the tubercle bacilli.

We do not know, or do not know thoroughly:

1. The biology of the parasite, how simple or complex, constant or variable is its life cycle.

2. The significance of variations in the parasite, as the human or bovine strains, their relation to each other and to the production of disease in various hosts.

3. The explanation of virulence and resistance, and the relative importance of these factors and of dosage in the development of the disease.

4. The rôle of family and racial heredity.

5. The relative importance of various modes of exposure and portals of infection.

6. The truth about such alleged predisposing factors as influenza and children's diseases.

7. The effect on the disease of syphilis or other coexisting infections.

8. The physiology of defense, and the part played in it by body fluids and special cells (for instance, the various leucocytes), tissues (for instance, lymphoid), and organs (for instance, adrenal and thyroid).

9. The absolute and relative frequency of healed and active tubercle, and the amount of variation of these figures in different localities and classes.

10. The occurrence of healed tubercle among savage races, and in young children, to whom tuberculosis is a new disease.

11. The relation of infection and lesion to immunity.

12. The effect of mental states on tuberculosis.

13. The effect of tuberculin, and the indications for its use in treatment, as well as the indications for rest, occupation and diet.

14. The possibilities of protective vaccination, and of chemical therapy.

15. The significance of mixed infections, and the factors concerned in toxaemia.

16. The effect of the antituberculosis campaign and the relative importance of its various phases.

17. The clinical aspects of childhood infection, how to recognize this beginning infection, and how to safeguard the children until its arrest.

The list is not exhaustive, but serves to illustrate the little we know and the much we need to learn.

THE NEED FOR FURTHER RESEARCH

All will I believe agree that epoch-making discoveries in this disease have been limited to those of Laennec on the unity of the disease and the methods of its diagnosis, of Villemin on its infectiousness, of Koch in the discovery of the tubercle bacillus, of Pirquet in the application of tuberculin to the skin test, and of the surgeons and physicians who first applied the principles of rest and fresh air.

It has seemed remarkable that in the past half century there have not been a score of laboratories in the world engaged in research work to add to our knowledge of tuberculosis. The tendency of the times has been to investigate diseases which gave promise of quicker solution, and to leave these more difficult problems to a few undaunted workers, themselves often its victims. Education of the people and of the profession, in what we know of the disease, must still be our first and foremost weapon. We cannot however stand still in our lack of knowledge, but we must definitely encourage progress by research.

We read that "Experiment, experiment" was the burden of Roger Bacon (1210–1293), but not till the fifteenth century did his ideas produce their first fruits, when Leonardo da Vinci could say, "Experiment never deceives. It is only our judgement that goes astray, when we make deductions not inherent in the former." A "Renaissance" is badly needed in our research efforts in tuberculosis and it is to be hoped that just as, when "the sixteenth century dawned, and the world recovered from the storm of social trouble that had followed the pestilences of the fourteenth century, Western Europe broke out into a galaxy of names that outshine the utmost scientific reputations of the best age of Greece," so may we be privileged before long to encourage and proclaim a new Jenner or Pasteur in vaccination against this disease, if not a Behring or Ehrlich in its cure.

In the first presidential address of Dr. Trudeau, we read, "The scientific study of tuberculosis offers so broad a field, and one requiring observations extending over such long periods of time, that special permanent endowments solely for researches in tuberculosis, which would enable experimentation in this field to be carried on continuously through a number of years, are greatly needed." And again, "But it is mainly to laboratory research work that we must look for the solution of many of the as yet unsolved problems of tuberculosis, and for the advance in our methods of prevention and treatment."

The nations recently engaged in the World War unhesitatingly poured out their wealth to find new methods of destruction and to counter such methods of their enemies, yet not one has thoroughly encouraged any attempt to counter the terrible devastations of the tubercle bacillus, whose victims number hundreds of thousands yearly in almost every civilized country.

You will learn with pride that during the past year The National Tuberculosis Association for the first time in its history has attempted to aid and encourage a few laboratory workers whose efforts to increase our knowledge have given promise. Some support has been given previously to research of a sociological nature. This is only a beginning, yet it may serve to stimulate others to give help. What more glorious service to mankind could many rich men or women be connected with than the providing of money for scientific work in tuberculosis? "But," to quote Wells again, "as scientific men tell us continually, and as 'practical' men still refuse to learn, it is only when knowledge is sought for her own sake that she gives rich and unexpected gifts in any abundance to her servants. The world of to-day is still much more disposed to spend money on technical research than on pure science. The business man of today still thinks of research as a sort of alchemy."

SOME INDIVIDUAL POINTS OF INTEREST

So much for my main thesis, the limitations of our knowledge and the great need of increasing it. Some points of special present or perennial interest now deserve individual mention.

Sixteen years ago, in the address referred to, Trudeau declared his faith that a method of preventive vaccination would be found. We find this same hopefulness expressed in the presidential address of Dr. Vaughan last year, as well as his hope that the National Association would be able to help such investigators financially. Colonel Bushnell also, in his recent excellent work on Epidemiology, expresses the belief that in time nature's rough and wasteful methods of protective vaccination may be replaced by a safe and scientific method of inoculation.

There has been recently in this country, and in other parts of the world, wherever there is not decided malnutrition, an unusual drop in the death rate from tuberculosis. At present we have no explanation to offer for this phenomenon. We may at least claim that part of this decline is due to the work of the National Tuberculosis Association. We have confirmation of this conjecture in the reports of The Metropolitan Life Insurance Company. By measures similar to those of our association, this company has greatly reduced the morbidity and mortality from tuberculosis among its policy holders. It is exceedingly difficult to state to which part of the work of the Association such benefits may be due. Some will attribute them to the campaïgn and gospel of right living, rather than to antispitting laws, registration, dispensaries and sanatoria. While it is true, as Baldwin said in his presidential address of 1916, that our work, like all practical work, occasionally misplaces its emphasis, yet there can be no doubt that the lines followed in the antituberculosis movement by The National Association are sound in the main. Too much effort cannot be made to see that the teachings of this Association permeate and repermeate every hamlet in the country, and too much praise cannot be given the faithful sociological and medical workers who have already been the pioneers.

While the Association is teaching, it should also be learning. One of the most certainly and permanently valuable branches of our work, in my opinion, is the collection of accurate statistical data, critically analyzed, for these have hitherto been painfully wanting. The pioneer Framingham Survey has already proved not only an adventure but an achievement.

In taking the histories of intelligent patients we are more and more struck with the occurrence of family infection in tuberculosis. There can be little doubt that repeated infection in childhood from a tuberculous father or mother must be more guarded against in the future than it has been in the past. Of four hundred and fifty cases examined in our recent records, over fifty per cent give a very definite account of family exposure in childhood. We have evidence from the laboratory which demonstrates the chronicity of disease brought about by repeated irregular infection. That many children so exposed may not suffer from the later accidents of environment and strain necessary to activate their disease, is no doubt true. Yet many of such exposed children will give at least X-ray evidence of greater infection than those not so exposed.

The percentage above quoted would be far greater did all patients know the truth, and did all patients tell the truth, about their family history. Only recently a patient was brought to me whose family history was said to be negative. Later I learned from the wife that the patient's father had died of tuberculosis, but that the patient thought if he reported this our prognosis would be graver. How often we find too that examination of the parents of patients with negative family history will disclose "carriers," who in many instances have open pulmonary tuberculosis of many years standing.

The Oeuvre Grancher of the French, with its principle of isolating healthy children from tuberculous parents, founded on Pasteur's discoveries regarding disease in silk worms, is without doubt one of the most effective efforts ever made against tuberculosis. More and more we must protect children against repeated infection while their immunity is being developed, and the ubiquity of "carriers" must be more heeded.

Our war experience seems to have stimulated interest in one of the gaps which the rapid development of the campaign against tuberculosis has left. Vocational training and rehabilitation are at present arousing considerable discussion. Among the large group of tuberculous patients under thirty who have not yet made a settled place for themselves in the world, industrial colonies may well prove useful. Needless to say, however, their development must be carefully considered, and they must grow and prove themselves as other factors have.

Possibly it is unfortunate that with the loss of enthusiasm of war time, we are unable to continue along the lines set by Colonel Bushnell in the handling of the Army tuberculosis problem. The routine examination of young adults, the opportunity for the study of tuberculosis occurring in all sections of the population, the special instruction in tuberculosis of large groups of medical men, and the efforts to provide adequate hospital and sanatorium facilities, are a few of the accomplishments of the army plan which were beginning to bear fruit.

However the Public Health Service and the National Tuberculosis Association are working most earnestly to build on that experience and to fit to the civilian requirements many of the broad plans conceived and instituted in the army.

CONCLUSION

At the end of this review of the great deficiencies in our knowledge of tuberculosis, and of the great interest and importance of rational understanding of the disease, I cannot do better than to quote from a recent address of Theobald Smith, by far the most able and eminent student of tuberculosis whom this country has yet produced:

> On account of the futurity of research it asks of us a certain amount of faith in its value and promise. It is supposed to attack the still unknown or mold the still vague and undefined. No one can promise definite results in definite directions. Results always will come after faithful work on the part of talented workers, such as will amply repay the public for the outlay, but the objective aimed at may not have been reached. We think a certain result, usually in our favor, should be reached. But our thinking so does not create a reality. If our thoughts and desires could anticipate results there would be no need of going through the elaborate and time-consuming process of getting at such results by experiment. Subsidizing research is like planting trees to be used by our successors. It is for the benefit of those who come after us, and in so far it is one of the high achievements of the present type of civilization.

This, then, is the opportunity that lies before this Association, and which I wish to emphasize and insist upon in laying down the office with which you have honored me. Let us not become smug, self-satisfied, routine men. Let us keep our senses alert for new knowledge, and not close our ears to the voice that Kipling's Explorer heard:

Something hidden. Go and find it. Go and look behind the Ranges—
Something lost behind the Ranges. Lost and waiting for you. Go!

The author wishes to thank his co-workers, Dr. C. T. Ryder, Dr. A. M. Forster and Dr. J. A. Sevier for valuable aid and criticism in the preparation of this address.

A COMPARATIVE STUDY OF THE PATHOLOGY AND X-RAY DENSITIES OF TUBERCULOUS LUNG LESIONS

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The object of this study has been to determine what cellular pathology underlies the various densities seen upon the lung plates of our tuberculous patients; to determine if possible which densities are found in healthy lungs; and to determine if "peribronchial and perivascular thickening" is generally associated with tuberculous lesions along such trunks.

One of us (Dunham) has previously called attention to the fan found on the X-ray plate in adult tuberculosis, its relation to the lymphatic circulation, and the chief cause for its formation due to the limitation of exudate and other pathological changes by the trabeculae. But the fan does not cover all the pathological lesions of tuberculosis and is in itself alone not pathognomonic of the disease.

It is most important to know whether tissue which shows no abnormal densities is free from tuberculosis. "Perivascular and peribronchial tuberculosis" has been appearing more and more in our medical literature, so that it is especially important to know whether it has a sound pathological foundation based upon the study of sections made from lungs previously X-rayed or whether it is being read into lung plates simply from an academic knowledge that such pathological changes existed.

An unusual number of illustrations is necessary because it is almost impossible to convey by word picture what one sees upon an X-ray plate.

It is desired that the presentation of this subject will help to place X-ray chest examinations, so far as pulmonary tuberculosis is concerned, upon a firmer pathological foundation and that the tuberculosis specialist and the roentgenologist will learn to look upon abnormal densities within the lung as indicative of definite pathological changes which require careful study. It is hoped that X-ray diagnosis of pulmonary tuberculosis will be more generally amplified, so as to state the location, extent and character of the lesions and that etiology will be less specifically emphasized. It is further hoped that the X-ray diagnosis will not be accepted blindly by the clinician, but will be used in conjunction with other laboratory findings, to interpret and correct physical signs and that whenever possible the postmortem will be used to study the limitations of all these methods, which are used to arrive as a diagnosis.

In this way will the usefulness of the X-ray picture be brought to its greatest value and physical findings will be placed upon a firm foundation when signs are interpreted in the light of X-ray densities. Then our patients will have the benefit of a more accurate and more complete diagnosis from which a better prognosis can be deduced.

The value of a physician's advice to his patient suffering from pulmonary tuberculosis is directly proportional to the accuracy of his prognosis. To prognose such a case we must accurately determine the extent and character of the lesions and estimate the reaction of fibrous repair which has or will occur. Realizing that we may appear trite, we nevertheless repeat that a comprehensive understanding is necessary. The history past and the present; the clinical condition of the patient; the chief complaint; the location and diagnosis of other lesions and infections; especially the pathological nature and extent of the pulmonary lesions; all must be known and considered in conjunction with the age of the patient and the physical signs, if a prognosis is to have value. What we wish to emphasize is that in our opinion no method has ever been found which will give nearly so accurate a picture of lung pathology during life as the X-ray plate. But the densities upon the plate suggesting these pathological lesions must be studied by the intelligent and trained mind of one who brings his knowledge of the case and the disease to bear and who frankly interprets his physical findings in the light of abnormal X-ray densities. Thus can a prognosis be deduced which has real value and a step in advance will have been made, but the prognosis will not always be correct. So it is hoped that a careful study of these cases and their illustrations will lead to a more accurate and more general study of X-ray densities and that what we have found to be of practical value may be useful to others.

It was of the greatest interest to all concerned during the progress of this research to note the accuracy with which normal lung tissue could be detected from the X-ray plate. It was of equally as much interest that we positively determined that "thickened trunks" and the so called "peribronchial and perivascular thickening of tuberculosis" are not necessarily associated with tuberculosis even when there is apparent studding along these trunks. It must not be concluded from this that we consider that peribronchial and perivascular tuberculosis does not exist. We know that it exists; but maintain that it cannot be diagnosed from an X-ray plate.

The material for this research was obtained at the Cincinnati Tuberculosis Sanatorium and the pathological study was prosecuted jointly at the University of Wisconsin. Professors W. S. Miller and C. H. Bunting have rendered every possible assistance and Dean Bardeen has been most generous. Dr. Bunting has read most of the pathological sections and Dr. Miller has directed the technique for the study of serial sections. Dr. Miller's knowledge of the normal lung structure was of constant value and enabled us to avoid many errors. The study has been in process of development since the beginning of 1915. Its presentation has been delayed but greatly benefited by the war.

One of us (Dunham) has recently published *An X-ray Classification of Pulmonary Tuberculosis* and this research is part of the pathological basis of that classification. A study of these cases and their illustrations will also show the cellular pathology underlying the abnormal densities better than any description. The classification was found of the greatest value in more than 5000 cases studied at United States Army General Hospital No. 19 where nearly 150 cases came to autopsy. Further, 146 cases were studied at the Cincinnati Tuberculosis Sanatorium in 1920 with 73 autopsies. Thus we feel that we are not presenting a purely theoretical thesis; but assure our readers that there are many problems remaining for future solution. In many cases chest plates have been studied before death, but in other cases this was impossible. This, however, is not a study to show what diagnoses have been made but to determine what diagnoses are possible from abnormal densities.

Technique. The lungs are removed from the thorax with great care so as to preserve the pleura intact; otherwise the lungs cannot be inflated. At times the parietal pleura has been removed with the lungs because of adhesions. Often more than an hour is consumed in removing the lungs. After the lungs are removed the lobes which have their pleura intact are inflated. Small pleural tears are closed by hemostats. A cork through which a tube is passed is securely tied in the trachea or bronchus and air is slowly pumped into the lung by a Davidson bulb. During this procedure the lung is so manipulated by the hand as to bring air into all parts of the lung and to fill all atelectatic areas.

Here we will break the logical order of presentation to explain and amplify the importance of proper inflation. Inflation is fundamental in a study of lung anatomy and pathology, especially when lung densities are to be studied by the aid of X-ray plates.

It has been stated that a cubic centimetre of caseous material cannot be detected when in the centre of a lobe, even if the lung is removed from the body. This may be true in a collapsed lung, especially if the lung has been cut to allow the insertion of the caseous block. But within the centre of a lung inflated to represent normal conditions a cubic centimetre of caseous material can always be recognized. Thus the greatest care must be given to proper inflation.

The lungs thus prepared are hung before or laid upon the plate changers and several sterescopic X-ray pictures are made. The time of X-ray exposure is just one-half that given to a chest plate, the spark gap, distance and milliamperage being the same.

The lungs are then deflated and 10 per cent formalin is run into them until they are distended as nearly as possible to their normal size. The trachea is then tied off and the lungs are placed, base up, in a jar of formalin, weighted in such a manner as to allow them to float free and harden without distortion of their shape. After forty-eight hours the lungs are removed from the formalin and placed in a similar manner in a jar of 90 per cent alcohol. In this way the tissues will remain soft. The formalin will have fixed the material so that a block can be removed from any selected area as chosen from the X-ray plates.

Large blocks are removed, imbedded in celloidin and cut. It is important to cut thick sections, because when the lung is hardened in its normal shape the air cells are open and easily penetrated by light. Thus fewer sections of a series need to be studied to determine the relation of a lesion to the anatomical structures. Serial celloidin sections were cut after the technique recommended and supervised by Dr. W. S. Miller. The sections were placed accurately in serial order, imbedded in large sheets of phytoxolin and stained in these sheets. They were then put into orders of groups and mounted in series on large slides. The stains used were hemotoxylin and eosin for some diagnostic slides, which also were cut thinner, and alum carmine or Weigert's elastic fibre stains for the series. The latter stains were used to bring out the elastic tissue, a method which greatly helped to identify anatomical structures which had been infiltrated by tubercles.

It was from one of these series that one of us (Skavlem), under the direction of Dr. Miller, built a wax model of a tubercle showing the relation to artery, bronchus and vein.

After all the blocks desired have been cut out of tle lung it is grossly sectioned but the usual pathological cuts are not followed. Instead, the lung is cut as nearly as possible along the main bronchi. This brings out the curious fan formation of the usual tuberculous lesion in the upper lobes of an adult case. In this way we find all the pathological changes suggested by the X-ray plate and careful cuts along the bronchi reveal any other lesions which may have been overlooked.

The following cases are grouped into types and each type is illustrated. Before we present the cases we wish to call attention to *An X-ray Classification of Pulmonary Tuberculosis*, so that the various types may be seen to fall into their respective places.

We also wish to emphasize the necessity of studying the distribution and character of lesions throughout all lobes, because taken alone the densities offer nothing characteristic in quality. Thus the density of an old infarct cannot be differentiated from an old tuberculous fan. Yet, when taken in conjunction with the whole lung such a differentiation can be made. Again, the densities of caseous bronchopneumonia, miliary tuberculosis and conglomerate tubercle may not be characteristic if a small area is considered, but when the entire distribution of the lesions throughout the lung is considered in the light of our knowledge of the spread of such lesions, a definite and characteristic picture is before us. So also, a single fan is neither characteristic in itself nor pathognomonic of tuberculosis. Any lung infection in which an exudate is thrown out may produce a fan, for the same anatomical reasons as its production in tuberculosis. But, due to the pathogenesis and spread of tuberculosis, which we know to consist of a series of repeated infections, either from without or within, fans of different densities are formed. Here again, viewing the lung lesions as a whole and seeing two or more fans of different densities, we are confronted with a characteristic picture.

We feel that with these points in mind a study of the cases will be of more value.

AN X-RAY CLASSIFICATION OF PULMONARY TUBERCULOSIS

The lung with its pathology is regarded as a whole to adopt the classification especially to X-ray work.

1. *Adult tuberculosis. Synonyms:* Secondary tuberculosis; nodose tuberculosis; apical tuberculosis; chronic fibroid tuberculosis; tuberculosis in the sensitized patient.

(A) Apical fibroid tuberculosis. Earliest findings, localized tuberculosis pneumonia; if lesion extends, chronic fibroid tuberculosis develops.

(B) Gelatinous and caseous bronchopneumonia (with apical lesions).

(C) Lobar caseous pneumonia (with apical lesions).

(D) Fibrous pleurisy; pleural exudate.

2. *Puerile or primitive tuberculosis. Synonyms:* Childhood tuberculosis; tuberculosis in the nonsensitized patient; focal tuberculosis.

(A) Primary lesion and tuberculous nodes.

(B) Miliary tuberculosis.

(C) Basal tuberculosis.

(D) Tuberculous caseous broncho- and lobar pneumonia (without apical lesions).

(E) Caseous pleurisy.

1. CASES OF ADULT TUBERCULOSIS

No. 1217. L. P. Age twenty-two. This case is an example of adult type with old lesion and cavitation in the apex and tuberculous caseous pneumonia throughout the rest of the lung. The fan of acute pneumonia at the base is definite and interesting, because of its differing in density from the caseous bronchopneumonia. This is brought out well also on the microscopic slides from blocks 2 and 3 (figs. 3 and 4).

X-ray reading of lung plates (see fig. 1). The plates show well the incisurae and point at which the bronchus to the middle lobe is given off from the main bronchus.

The prevailing lesion is caseous bronchopneumonia throughout the entire lung. In the upper lobe the areas of the vertebral and first interspace trunks are honeycombed with cavities. The remaining portion of this lobe shows a general scattering of caseous bronchopneumonia.

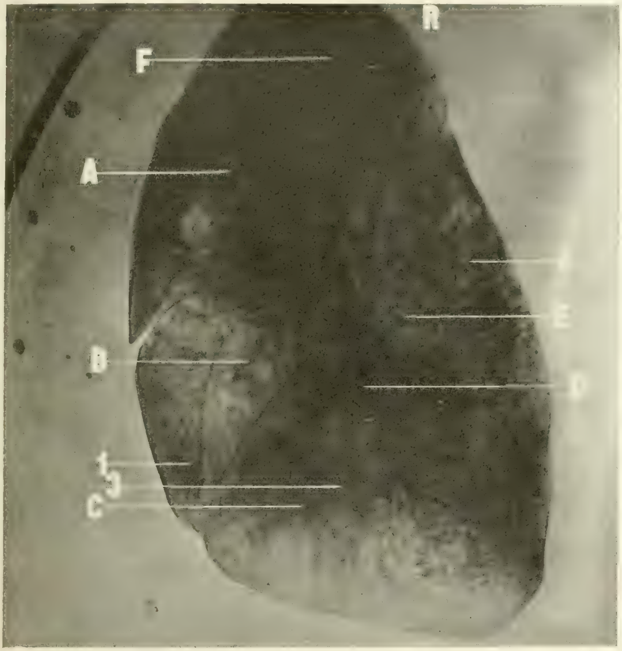

Fig. 1. No. 1217. X-Ray Plate of Right Lung

A—Upper lobe. *B*—Middle lobe. *C*—Lower lobe. *D*—Large fan of acute pneumonia. *E*—Caseous bronchopneumonia. *F*—Tube used for inflation. *1*, *2*, *3*—Areas of respective blocks.

The middle and lower lobes likewise show a general scattering of caseous bronchopneumonia. In the lower lobe is seen a large fan of pneumonia involving the anterior branch of the main stem bronchus. The traiangle does not reach the margin but does reach three surfaces, namely, anterior, diaphragmatic, and surface in the incisura. The density of this fan is different from the mottling of the caseous bronchopneumonia throughout the rest of the lung. (See fig. 2 for X-ray plate of chest.)

Gross pathological description. The apex of the upper lobe is entirely excavated by large tuberculous cavities. The rest of the lobe shows a general scattering of areas of tuberculous caseous bronchopneumonia and small yellow caseous nodules.

The middle and lower lobes show a general appearance similar to the upper lobe without cavitation. Along the anterior division of the main stem bronchus to the lower lobe the pneumonia is heavier and the areas are more confluent.

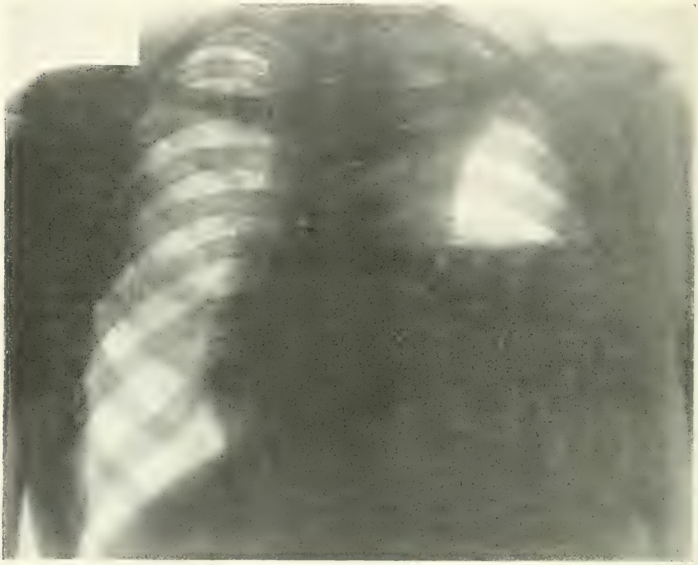

Fig. 2. No. 1217. X-Ray Plate of Chest

Hydropneumothorax on the left side. Fluid level reaches the seventh spinous process.

Right thorax: Caseous bronchopneumonia throughout the upper right. The middle right is infiltrated with caseous bronchopneumonia but to a less degree than the upper lobe. Nothing abnormal is made out in the lower lobe. The prognosis is desperate on account of the destruction of the left lung and the caseous bronchopneumonia on the right side.

Note: This patient died one year after these plates were taken.

The walls of the bronchi throughout the lung show some thickening.

Microscopic pathology.

Block 1. Location: Tip of middle lobe at end of main stem bronchus in area showing fan shaped mottling.

Reading: Pleura is edematous, thickened and shows old hyaline fibrin on the surface. The lymphatics are greatly dilated. Lung tissue shows many areas of tuberculous bronchopneumonia with well marked central caseation.

Block 2. Location: Apex of lower lobe, showing coarse diffuse mottling.

Reading: Pleura is thickened and shows fibrinous exudate. The lung tissue shows many areas of tuberculous caseous bronchopneumonia. Under the pleura these areas are close together, the intervening alveoli showing a gelatinous pneumonia. Deeper in the section the gelatinous pneumonia is somewhat less well marked (see fig. 3).

Block 3. Location: Lower lobe on diaphragmatic surface in area of fan.

Reading: Pleura shows fibrinous exudate and some definite tubercles. The septa show edema and the lymphatics are dilated. The major part of the section is occupied by almost confluent areas of acute bronchopenumonia. The cellular exudate is rather scanty in the involved alveoli and the serous exudate is well marked. Intervening alveoli show considerable edema and some desquamation of cells. Toward the inner part of the section are two large caseous interstitial conglomerate masses with slight pneumonic exudate about them and with some thickening of the adjacent lung framework (see fig. 4).

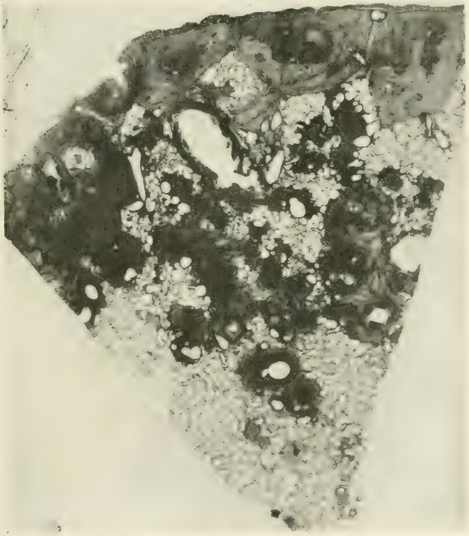

Fig. 3. No. 1217. Microscopic Section through Block 2

No. 1206. C. H. Age forty-seven. This case is typical of far advanced tuberculosis with heavy fibrosis, caseation and destruction in the apex and more recent pneumonic process in the lower lobe. The isolated fan in the lower lobe is interesting in its identical density with that which might be caused by an infarct. Microscopic section 6 shows very well the limiting of a pathologic process by a septum.

X-ray reading of lung plates (see fig. 5). The pleura is thickened over the greater part of the lung but especially over the apex and upper posterior part of the lower lobe and in the incisura.

The upper lobe shows old chronic tuberculosis with caseation, fibrosis and extensive cavity formation. The heaviest consolidation and greatest cavity formation are found in the posterior divisions of the vertebral first and second interspace trunks. The anterior division of the vertebral trunk shows some normal lung tissue. The lingual tip shows an abnormal lobation. The main stem bronchus to the lingual tip is prominent and in its proximal extent shows scattered areas of caseous bronchopneumonia on both sides, while near its end the lung tissue is comparatively normal.

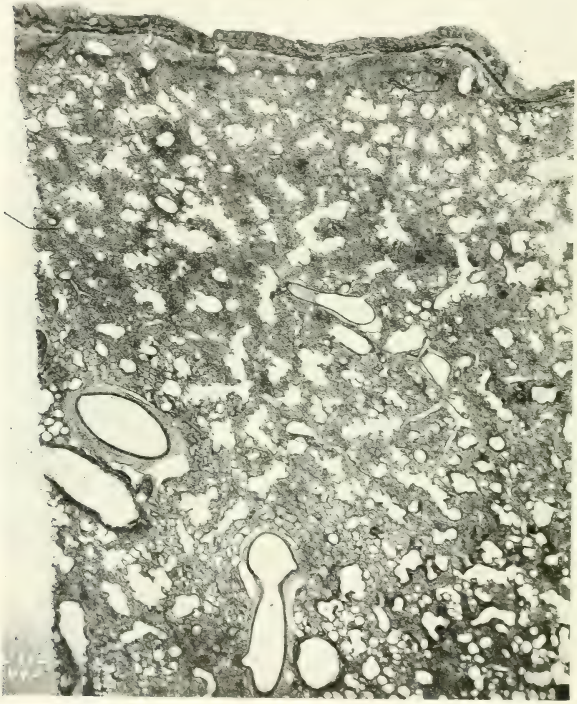

FIG. 4. NO. 1217. MICROSCOPIC SECTION THROUGH BLOCK 3

The apex and mesial part of the lower lobe shows heavy density due to massive caseation. On the lateral surface under an area of adherent pleura, between the middle and lower thirds of the lobe is found an isolated fan, probably due to caseation. The lower part of the lobe is comparatively normal. The main stem bronchus is thickened and prominent.

Gross pathological description. Upper lobe: The lung tissue supplied by the anterior division of the vertebral trunk is soft, air bearing and comparatively normal. The posterior portion along the posterior divisions of the vertebral first and second interspace trunks shows massive consolidation and great lung destruction. This portion of the lung is honeycombed with intercommunicating cavities of all sizes, the largest measuring 3 by 5 cm. The vertebral trunk in the extreme apex posteriorly shows the greatest destruction. The pleura over this portion of the lung is greatly thickened. The area of the anterior division of the first interspace trunk shows massive caseous consolidation with early cavity formation. The area of the anterior division of the second interspace trunk also shows considerable infiltration and consolidation with a small amount of air bearing tissue along the anterior margin.

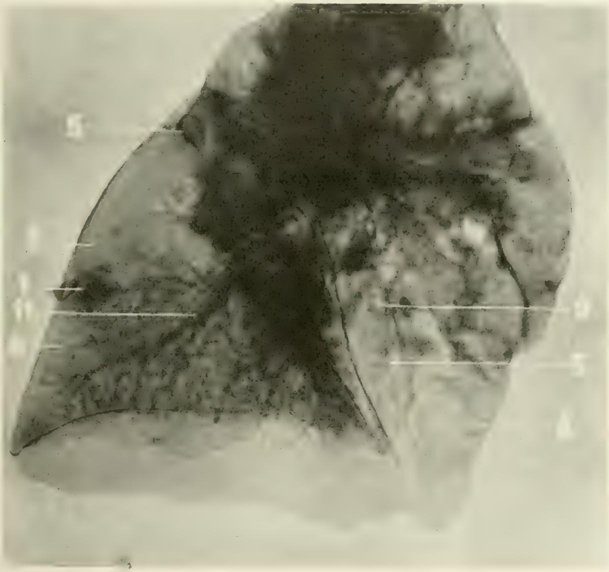

Fig. 5. No. 1206. X-Ray Plate of Left Lung

A—Lingual tip with abnormally exaggerated separation. *1, 2, 5, 6, 8, 9, 11*—Areas of respective blocks.

The lingual tip shows practically normal lung tissue at its tip but further in along the main bronchus on both sides there are scattered areas of caseous consolidation and heavy infiltration.

Lower lobe: The extreme apex and inner one-third of this lobe show massive caseous and fibrotic consolidation. Below the apex on the costal surface is an area of practically normal lung tissue while in the middle of the lobe on the posterior part of the costal surface immediately under the pleura (1) is an area of caseous consolidation. The lower part of the lobe is soft and shows little gross pathological change except marked thickening of the bronchi and connective tissue framework, with some areas of infiltration and patches of caseous bronchopneumonia near the fissure. The pleura over the upper and posterior part of the lobe is thickened. The pleural surfaces in the incisura are thickened and bound together by fibrotic adhesions, especially in its posterior third.

Microscopic pathology.

Block 1. Location: Fan seen on plate on lateral surface of lower lobe.

Reading: Caseous bronchitis, bronchopneumonia, some interstitial tubercles, slight peripheral edema, some edema of septa and pleura.

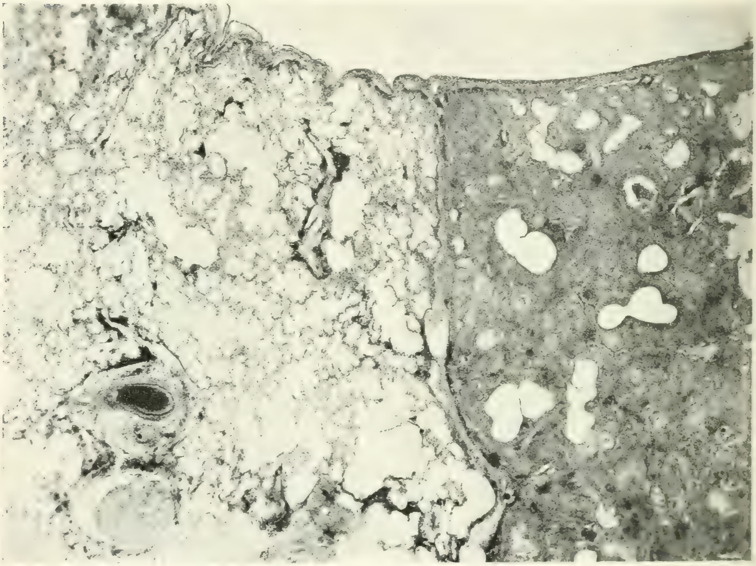

Fig. 6. No. 1206. Microscopic Section of Block 6

Block 2. Location: Normal appearing area just above block 1.

Reading: Practically normal. Some chronic bronchial cellular exudate; slight edema. No positive tuberculosis.

Block 5. Location: Incisura between upper and lower lobes in outer third of lung just above normal spot.

Reading: Lower side shows some normal lung, but also an area of caseous bronchopneumonia extending to the incisura at two points but most marked at some distance from the incisura. Above the incisura the lung is heavily involved showing old caseous areas both interstitial and pneumonic. Edge of small cavity is seen. There is marked induration of lung framework with atelectasis, slight emphysema in other parts and one area of hemorrhage.

Block 6. Location: Lateral surface of lingual tip.

Reading: One extensive area of caseous pneumonia, also several small areas. Lung framework practically normal. Some edema of septa (see fig. 6).

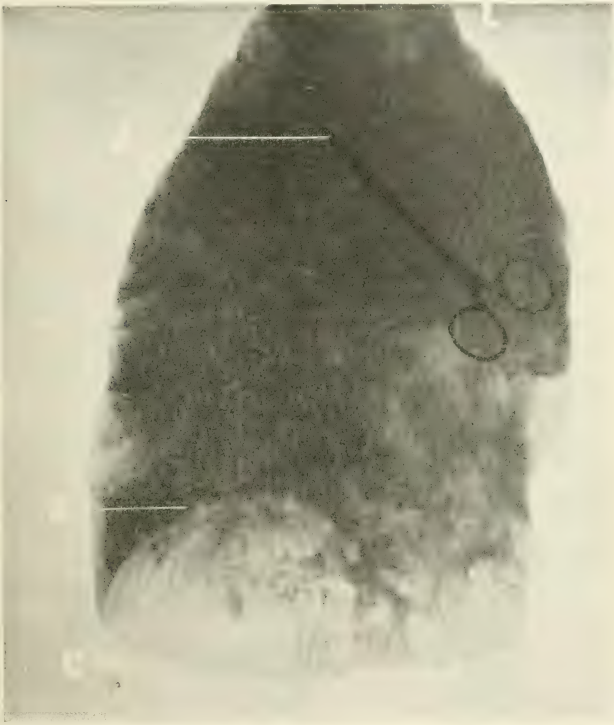

Fig. 7. No. 1228. X-Ray Plate of Left Lung

A—Artery forceps used to close tear in pleura. *B*—Anterior basal margin. *C*—Posterior basal margin. *1*—Area of block 1, showing three densities.

Block 8. Location: Just below block 1 on lateral surface, showing mottling.

Reading: Section shows several areas of bronchopneumonia in which exudate consists almost entirely of polymorphonuclear leucocytes, without caseation, surrounded by areas of edema. Marked congestion of vessels, slight hemorrhage.

Block 9. Location: Deep in lingual tip, 2 inches above the extreme tip.

Reading: Section shows chronic interstitial tubercles, irregular sclerosis and an extensive area of caseous pneumonia close to the pleura.

Block 10. Location: Lymph node at the hilum.

Reading: Scattered miliary and conglomerate tubercles.

Block 11. Location: Bifurcation of main stem bronchus to lower lobe in midzone.

Reading: Calcification of cartilages of larger bronchi. Lymphatics dilated, edema of perivascular and peribronchial connective tissue. Close to largest bronchus is an area of old caseous interstitial tubercles with sclerosis of lung framework and some caseous pneumonia in vicinity.

No. 1228. A. R. Age thirty-three. This is a most interesting case to study and verify the degree of density caused by pathological changes in the three densities located at the base along the diaphragmatic border. The microscopic section is very unusual in showing three distinct pathological conditions side by side, each verging on the other by sharp demarcation. The distinctive densities produced by the conditions are seen on the X-ray plate and make a splendid study of the degrees of density produced by each such pathological change.

X-ray reading of plates no. 1227 and 1228 (see fig. 7). *Left lung:* In the upper lobe there are some old fibroid lesions containing cavities in the apex and tuberculous pneumonia occupying the rest of the upper lobe except for a small area in the lingual tip which is emphysematous. The upper half of the lower lobe shows a lesion similar to the lower part of the upper lobe, confluent caseous pneumoia. The lower part of the lower lobe contains some air bearing tissue. Numerous cavities are seen throughout the lower lobe. The only normal portion of this lung is seen along the diaphragmatic margin, occupying the anterior half. Three distinct differing densities are noted in this area. The most anterior of these densities suggests lobular caseous pneumonia. The middle, just posterior to this along the margin, is comparatively normal. The third density is immediately posterior to the normal density and suggests acute pneumonia or hemorrhage without caseation. Below the vertebral and first interspace trunks of the upper lobe, the densities throughout the left lung are obscured by the so called snowflake appearance which indicates gelatinous bronchopneumonia, acute pneumonia or hemorrhage.

Gross pathological description. The upper lobe is practically consolidated, except the lingual tip, with tuberculous caseous pneumonia and large caseous tubercles. On the anterior margin is a linear area of confluent tuberculous caseous pneumonia of more uniform consolidation than the areas about it. In it is a fair sized cavity. The lingual tip is comparatively normal.

Lower lobe: in its apex and posterior part shows the same general consolidation with caseous pneumonia. The anterior portion of the lobe shows a pneumonic process of lesser caseation and consolidation. On the lateral surface extending to the inferior margin are two areas of pneumonia, separated by an area of comparatively normal lung.

Microscopic pathology.

Block 1. Location: Inferior margin of the lateral surface of the lower lobe.

Reading: One edge of the sections shows numerous areas of caseous and gelatinous bronchopneumonia, also several interstitial tubercles. There is considerable induration of the lung about these areas. The middle third of the section shows edema but otherwise the lung tissue is comparatively normal. The upper third of the section shows a heavy pleural scar. Some distance beneath the pleural surface there are numerous areas of acute bronchopneumonia without caseation, with a scanty cellular and considerable serous exudation (see fig. 8).

This section is very unusual in showing three distinct pathological conditions side by side, each verging on the other by sharp demarcation. The distinctive densities produced by the conditions are very plainly seen side by side on the plate and make a splendid study of the degree of density produced by each such pathological change thus: (a) heaviest density (A) is produced by "areas of caseous and gelatinous bronchopneumonia, also several interstitial tubercles. There is considerable induration of the lung about these areas;" (b) middle area of least density (B) or comparatively normal, is produced by "middle third of the section, shows edema but otherwise the lung tissue is comparatively normal;" (c) lesser density (C) is produced by "numerous areas of acute bronchopneumonia without caseation."

No. 1211. W. H. Age forty-nine. This case is peculiarly interesting because of the numerous curious thin walled cavities. These do not have the appearance of typical tuberculous cavities and are probably due to a mixed infection, such as influenza, causing rapid lung destruction in the tuberculous areas.

X-ray reading of plates nos. 1210 and 1211 (see fig. 9). *Left lung:* In the apex and the upper third of the lower lobe are two large areas of homogeneous density, honeycombed with cavities. These are characteristic of tuberculosis and suggest usual caseation. Throughout the upper lobe, except as described, including the anterior branches of the first interspace trunks and the second interspace trunks and the lingual tip, the predominant lesions are numerous, thin walled cavities not suggesting tuberculous lesions, but probably the result of other infection such as influenza. There is a haziness, which might be accounted for by tuberculous pneumonia, in the anterior branch of the first interspace trunks and to a lesser extent in the second interspace trunks. The only normal lung tissue in the upper lobe is at the extremity of the lingual tip. In the lower lobe with the exception of the upper third as described, the anterior half is honeycombed with cavities similar to those seen in the upper lobe. These are probably due to influenza but the cavities are of larger diameter. The anterior and lateral border of the lower lobe is the only part not involved. In the posterior half of the lower lobe, below the heavy tuberculous densities, there are numerous tuberculous fans scattered throughout the lung tissue which is otherwise only slightly infiltrated.

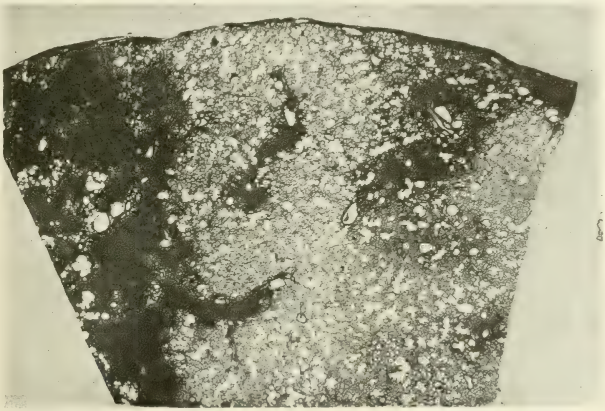

FIG. 8. NO. 1228. MICROSCOPIC SECTION THROUGH BLOCK 1

Gross pathological description. Upper lobe: is almost entirely involved in confluent caseous tuberculous bronchopneumonia with numerous thin walled cavities of various sizes scattered throughout all parts of the lobe. There is some dilatation of the bronchi. The consolidation is heaviest in the area of the posterior branch of the vertebral trunk. The only normal lung tissue is found in the lingual tip and immediately along the anterior margin.

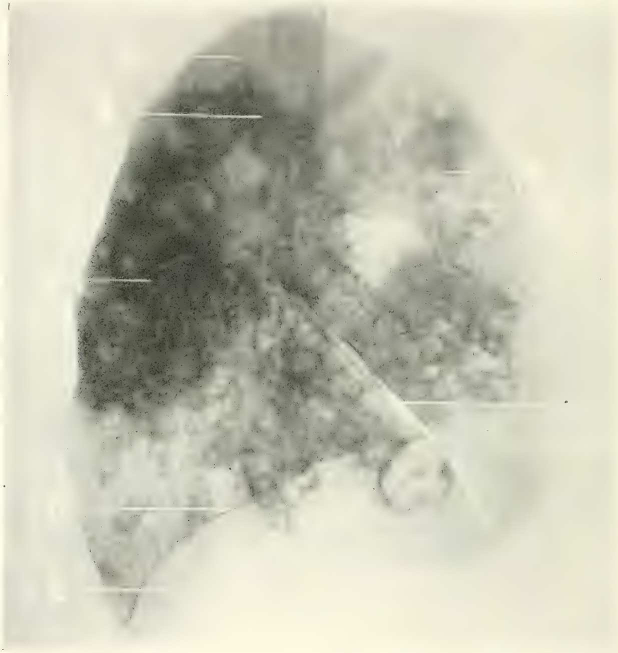

FIG. 9. No. 1211. X-RAY PLATE OF LEFT LUNG, TRANSVERSE EXPOSURE

A—Lingual tip. *B*—Caseous lymph node. *C*—Incisura. *D*—Anterior basal margin. *E*—Posterior basal margin. *F*—Pneumonic lesion occupying upper one-third of lower lobe. *1, 2, 3*—Areas of respective blocks.

Lower lobe: presents exactly the same condition as the upper one. The heaviest consolidation is in the apex of the lobe while the lower third posteriorly presents comparatively normal lung tissue.

Microscopic pathology:

Block 1. Location: Upper lobe in area of first interspace trunk anteriorly.

Reading: Marked congestion of lung and pleura. Extending from the pleura into the lung is a large cavity containing pus cells in heavy masses. The walls of the cavity lack granulation tissue. At some points the wall of the cavity is continuous with a heavy cellular exudate which fills adjacent alveoli. There is no caseation of the exudate or of the walls of the alveoli adjacent to the cavity. Patches of pneumonia occur in the vicinity of the cavity.

Block 2. Location: Upper lobe just below block 1 in area of second interspace trunk.

Reading: Section shows a cavity similar to block 1. There is more extensive peripheral pneumonia (see fig. 10).

Block 3. Location: Upper lobe in area of vertebral trunk anteriorly.

Reading: Section shows an extensive area of tuberculous caseous pneumonia with interstitial tubercles and pulmonary sclerosis extending from the pleura in a rough wedge into the lung.

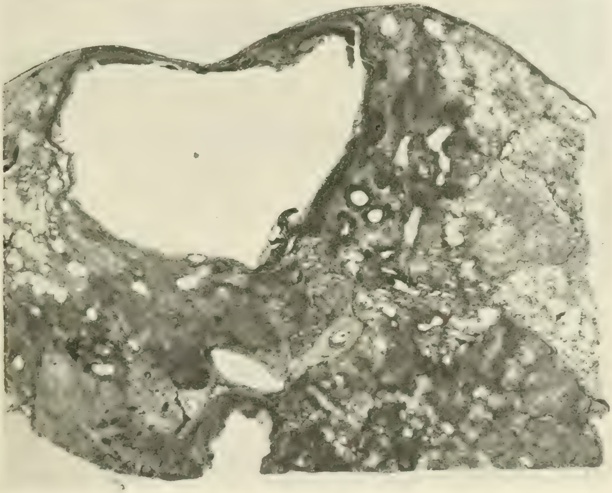

Fig. 10. No. 1211. Microscopic Section through Block 2

Note: The multiple thin walled cavities are apparently due to a mixed infection with rapid destruction in the tuberculous area.

No. 1060. N. H. This is a typical case of adult fibroid tuberculosis.

X-ray reading. No. 1061: The left lung has rotated so as to present a median view with lateral surface toward the plate. Thus the incisura lies in a plane between the tube and plate. In the upper left lobe on the vertebral trunk under a scar is seen an old tuberculous lesion with calcification just below. In the region of the first interspace trunk are a few dots of densities, some of which are calcified and healed. Numerous fine dots are seen near the pleura in the lower lobe extending back from the middle of the incisura. Good bronchial tree. No active tuberculosis in this lung, and only tuberculosis lesion is found in limited area of upper lobe. Right lung is not inflated. Anterior surface to the plate. Upper lobe is destroyed by cavities.

Gross pathological description. Upper lobe, left lung: In the area of the anterior division of the first interspace trunk, at the anterior margin under an area of thickened pleura is found an old typical pigmented, caseofibrous tuberculous scar, with calcification in its centre. The scar measures 1.5 by 2.5 cm., has a cheesy material and some calcification in its centre with a thick fibrous wall, from which radiate out fibrous bands into the surrounding lung tissue. The rest of the lobe appears normal except for thickening of the bronchial walls and connective tissue frame work of the lung.

Lower lobe, left lung: Except for congestion and some hemorrhage at the base posteriorly this lobe appears practically normal. There is thickening of the walls of the bronchi and several small areas of calcification are found in the walls of the larger bronchi of the anterior divisions of the main stem. The pleura is not thickened and the lobes are not bound together. The pleura and entire lung substance show considerable pigmentation.

Right lung: The pleura is greatly thickened by a very firm fibrous layer over the entire lung, except the anterior portions of the upper and middle lobes. At the base the pleura measures 3 mm. and at the apex 5 mm. with a lesser thickening over the costal surface except at the incisura. All lobes are firmly bound together by extensions into the incisurae of the same fibrous thickening. The lymph nodes at the hilum are large, heavily pigmented and show some caseation. The upper lobe is heavily pigmented and massively consolidated with caseation and fibrosis except at its anterior margin, where there is some air bearing tissue. In the extreme apex is a large cavity 3.5 by 2.5 cm., and another slightly smaller cavity just below it. The bronchial walls and septa are very markedly thickened. The middle lobe is soft and air bearing and, except for some congestion and thickening of the bronchial walls, it appears normal. The lower lobe shows no gross evidence of tuberculosis. There is extreme congestion and an area of hemorrhage at the apex. The walls of the bronchi are also thickened.

Microscopic pathology:

Block 1. Location: Cardiac surface of tip of upper left lobe.

Reading: Marked edema of pleura and septa. Lymphatics dilated, slight edema of lung. Section in general is normal. There is a small area of acute bronchopneumonia.

Block 2. Location: Main stem bronchus to lingual tip, near the hilum.

Reading: Marked edema of connective tissue around the larger vessels and bronchi. Some pulmonary edema of acute bronchopneumonia, slight sclerosis and anthracosis.

Block 3. Location: Second interspace trunk at hilum.

Reading: Lymph node shows great amount of anthracosis. Large bronchus shows slight calcification of the cartilage in its walls with some edema of the wall and adjacent lung tissue. No tuberculosis.

Block 4. Location: Just above block 3.

Reading: Edema of connective tissue around the vessels and bronchi, with some pulmonary edema. A few areas of acute bronchopneumonia and some sclerosis.

Block 5. Location: Anterior margin of upper lobe in area of density seen on plate.

Reading: Large caseous and calcified pigmented masses, cholestrin crystals also present surrounded by heavy connective tissue. Typical old tuberculous scar.

No. 1261. F. McC. This case is another of the adult type with old apical lesions and more recent tuberculous pneumonia below. The most interesting points in these lungs are the fans of pneumonia in both lower lobes, typical of aspirated caseous pneumonia.

X-ray Reading: All lobes are heavily involved with tuberculosis. Both upper lobes are honeycombed with cavities which are larger on the left side. Four calcified areas appear to circle the left bronchus at its bifurcation. The largest mass is seen just external and superior to the bronchus. A small mass lies anterior and superior to this large one. Mesial to the left bronchus just opposite to the large calcified area is a small line-like calcification apparently in the bronchial wall. Below this and posteriorly, but internal to the main bronchus of the lower lobe, is a fourth area of calcification which is second in size. In the lower left lobe is seen a triangle of increased density, which extends toward the base involving the base and lateral margin, which suggests aspirated tuberculous bronchopneumonia. In the lower right lobe not far from the mediastinal surface is seen a density which extends posteriorly toward the base. This density is cloudy and suggests a more acute involvement. Lateral and anterior to this on another branch of the main stem bronchus is seen a more flocculent triangle which suggests heavier tuberculous bronchopneumonia.

Right lung: Upper and middle lobes show gross involvement with tuberculous caseous bronchopneumonia and extensive cavitation. Large caseous lymph nodes with calcification are found at the hilum of both lobes. Apex of the lower lobe shows the same general condition with a few small cavities. Scattered areas of tuberculous caseous pneumonia of lesser density are also found extending toward the base, especially near the mediastinal side.

Left lung: Upper lobe shows heavy consolidation with tuberculous caseous pneumonia and large caseous nodules. The entire lobe is extensively excavated by cavities. Along the main bronchus are found several old caseous calcified lymph nodes. The lower lobe shows tuberculous caseous bronchopneumonia and scattered tubercles of lesser density and not so confluent as in the upper lobe. There are a few cavities in the upper half of the lobe. Greatest consolidation of the caseous pneumonia is seen in the inferior lateral part of the lobe.

Microscopic pathology:

Block 1. Location: Lower left lobe along the main stem bronchus near the base.

Reading: There is marked anthracosis in the pleura. The lung tissue appears normal except for slight edema. One branch of the pulmonary artery shows a thrombus.

Block 2. Location: Lower left lobe along the main stem bronchus proximal to block 1 in triangular density seen on the plate.

Reading: Pleura is thickened and shows fibrous adhesions with congestion of the vessels. The alveoli in some places show heavy edema. One large bronchus is filled with a purulent exudate and in one branch shows loss of epithelium. Its wall is heavily infiltrated with large and small mononuclear cells and a few polymorphonuclear leucocytes. There is also some necrosis of the wall. Adjacent to the bronchus is a conglomerate tubercle with caseous centre and surrounded by some early tuberculous pneumonia, the alveoli being filled with fibrin, serum and mononuclear cells. A similar condition exists about an adjacent smaller bronchus.

Block 3. Location: Lower right lobe in area of fan seen on branch of the main stem bronchus.

Reading: The bronchi are filled with purulent exudate. The walls of the bronchi are heavily infiltrated with mononuclear cells. The lymphoid tissue is increased in amount. There is an increase in the peribronchial fibrous tissue, which also involves the adjacent alveolar walls. One connective tissue area shows an old hemorrhage with phagocytes containing hemosiderin. Adjacent to a large dilated bronchus is seen tuberculous pneumonia.

Block 4. Location: Lower right lobe in area of fan seen on the main stem bronchus, posterior and below block 3.

Reading: Section is quite similar to block 2. The bronchi show involvement and there are many well marked areas of tuberculous pneumonia.

Block 5. Location: Base of the lower right lobe on diaphragmatic surface.

Reading: Section shows purulent bronchitis. Near the tip of the section is seen a fresh conglomerate tubercle with adjacent infiltration of the lung framework with lymphocytes, and slight alveolar exudate.

No. 1170. G. G. This case is of the usual type of far advanced adult tuberculosis with old cavities in the upper lobe and more recent pneumonic process in the lower lobe, the apex of which shows the heaviest involvement.

X-ray reading: The upper lobe is contracted and shortened in that it occupies only one-half of its normal space. There are tuberculous lesions scattered throughout the entire upper lobe. Four definite cavities of various sizes can be seen. The largest one of these is just above the apex of the lower lobe and reaches the surface near the lateral surface of the upper lobe. The middle lobe is comparatively normal on its anterior border from about 5 cm. from the upper incisura to about 10 cm. from the lower incisura. Laterally the lobe is definitely infiltrated. The apex of the lower lobe shows an old lesion with a small cavity. The branches of the main stem bronchus at the base show infiltration with large flocculent masses of disseminated tuberculosis, apparently of the aspirated type of caseous bronchopneumonia.

Gross pathological description: The upper lobe shows several areas of old caseation and fibrosis with several large cavities all of which connect directly with bronchi. The intervening areas of lung tissue are comparatively free from consolidation or infiltration and are air bearing. At the end of the posterior branch of the vertebral trunk is found a large thick walled cavity measuring 2.5 by 2.5 cm. It is surrounded by heavy fibrosis, especially at the lower wall and is no doubt the oldest lesion in the lung. The fibrosis of its lower wall extends down to the fissure, which separates the upper from the lower lobe. On the anterior branch of the vertebral trunk is found a linear bronchiectatic cavity measuring 1.5 by 3 cm. On the anterior division of the first interspace trunk is found a cavity measuring 2 by 2.5 cm., underlying an area of pleural thickening and contracture. This cavity lies immediately behind the trachea on the picture. The second interspace trunk is presented as a circular area in the midst of the hilum shadow, as it lies on the same plane as the centre of the tube. At the end of this trunk is found another bronchiectatic cavity measuring 2 by 3 cm. Some of the anterior divisions of the second interspace trunk are markedly thickened and show up on the picture as circular areas. On the lower part of the anterior margin of this lobe is found a small area of old caseation and fibrosis, which lies just 2.5 cm. above the fissure between the upper and middle lobes. The lobes are bound together in the anterior third of this diffuse area by dense adhesions.

The middle lobe along its anterior margin is normal. In the centre of the lobe, about 5 cm. from the anterior margin and on the anterior surface, under an area of thickened pleura, is a small area of fibrosis and old caseation. Above this on the same surface is a scattering of small caseous nodules.

In the apex of the lower lobe, 1 cm. under the fissure, is found a small thick walled cavity, 1 by 1 cm. Adjacent to this are a few small fibrous areas. The lateral surface in its middle portion shows a general thickening of lung framework and a few scattered areas of caseation. The main stem bronchus is markedly thickened and at its extremity near the base is an area of caseous bronchopneumonia giving a "raisin on the stem" picture.

Microscopic pathology:

Block 1. Location: Lateral surface of apex of lower lobe in triangle about 3 cm. below cavity on the plate.

Reading: Pleura shows outer layer of heavy fibrin undergoing organization. Old fibrous adhesions also present. Pleura is slightly edematous. Blood vessels and lymphatics dilated, one small hemorrhage, moderate anthracosis. In several places adjacent to pulmonary septa there is dense infiltration of the pleura with lymphocytes. Septa show marked thickening due to recent cellular fibrous tissue development. There is some lymphocytic infiltration and moderate anthracosis. Alveoli are free from exudate save for a moderate amount of albuminous precipitate. In deeper part of section adjacent to a medium-sized bronchus there is a well developed conglomerate tubercle surrounded by a heavy mass of lymphoid cells. Close to this and probably continuous with it is a second group of tubercles in a pulmonary septum, close to a small vein and involving the lymph vessels. One tubercle is definitely within a lymphatic. The tubercles tend toward hyalinization rather than caseation.

Block 2. Location: Just below block 1 on the same surface.

Reading: Section in general similar to block 1, showing, however, about 2 mm. below pleural surface an oval area of caseation, with fine deposit of calcium about 2 by 1 mm. This shows considerable peripheral pigmentation and is encapsulated by cellular connective tissue. There is a general thickening of the septum in which this mass lies.

Block 3. Location: Few cm. below block 2 on same surface.

Reading: Lesion is same as block 2 plus conglomerate tubercle lying in septum close to pleural border. There is little caseation. Tubercle is thickly surrounded by lymphocytes. No alveolar edema.

Block 4. Location: Lateral surface of middle lobe showing fine dots.

Reading: Section shows an irregular group of tubercles extending toward an interlobular septum. One of these is hyaline; the others show some caseation. There is a slight alveolar exudate adjacent to the mass consisting of fibrin and large ana small mononuclear cells. Organization of the fibrin is beginning. Nearby is another small area of organizing pneumonia. A second conglomerate tuberculous mass lies adjacent to a pulmonary septum near the first described.

Block 6. Location: Lymph node at hilum.

Reading: Lymph node showing anthracosis and several miliary and conglomerate tubercles. No calcification.

Block 7. Location: Middle lobe immediate to hilum and on border of incisura between middle and lower lobes.

Reading: Thickened pleura, beneath which lies a number of old hyaline tubercles with heavy peripheral anthracosis and radiating bands of connective tissue. Near this the small bronchi contain a cellular exudate with an apparent destruction of the mucosa in places, with infiltration of the walls by mononuclears and with adjacent areas of tuberculous bronchopneumonia. There are also present tubercles lying external to the muscle coat of the bronchi in the lymphoid tissue.

Block 8. Location: Main stem bronchus to lower lobe, near hilum.

Reading: Section through the large bronchi, vessels and lymph node. Latter shows anthracosis but no tuberculosis. Bronchi show cellular exudate but there is no involvement of the wall. Adjacent to the largest bronchus are one or two conglomerate tubercular masses and two others at about 1 cm. distance.

Block 9. Location: Same as block 8, only continuation of the main stem bronchus towards the periphery.

Reading: Section through larger vessels and bronchi. At a distance from the vessels and bronchi are three tuberculous masses; one an old caseous encapsulated mass roughly 3 mm. in diameter; another an S-shaped group of hyalin and more recent tubercles; the third is a pigmented hyaline mass with adjacent recurrent tubercles.

No. 1273. E. W. Age nineteen. This case is another of the typical adult form, with old apical lesions and more recent tuberculous pneumonia below. It is interesting that in this lung the extreme apex is remarkably clear, but the old lesion was found in the apex of the other lung.

X-ray reading of chest plates no. 1214 (E. W.): Pneumothorax on the right side. The lung is collapsed but the apex is attached to the thorax by adhesions and the base is attached to the right lateral wall and the diaphragm. A large cavity is seen in the apex. No fluid is made out. Caseous bronchopneumonia is made out in all of the branches of the left upper lobe except the lingual tip. Nothing abnormal is made out in the lower lobe but a large portion of the lower left and the lingual tip of the upper left are obscured by the heart which is enlarged and pushed to the left. The prognosis is desperate on account of the caseous bronchopneumonia and the complete destruction of the right side.

X-ray reading plates nos. 1272 and 1273. Left lung: Type of lesions: Confluent caseous bronchopneumonia, probably secondary to apical tuberculosis on thse right side. In the upper lobe, especially in the first interspace trunks anteriorly, there are old scars that suggest that the lesions are not all recent.

Distribution of lesions: The apex is comparatively clear with a few scattered areas of increased density, most marked anteriorly. Caseous bronchopneumonia is seen throughout the first and second interspace trunks, most marked anteriorly. These densities are less confluent near the lower anterior margin of the second interspace trunk.

The lingual tip of this specimen forms an abnormal individual lobe which clearly marks out the area of the lingual tip of the upper lobe. In the upper part of the lingual tip, near the main stem bronchus, there is a dense area of confluent tuberculous, caseous bronchopneumonia, distributed so as to leave a central area of decreased density which might easily be mistaken for a cavity. The upper part of the lingual tip, just below the second interspace trunks, is infiltrated with caseous bronchopneumonia but is less dense than that just described. The dependent portion of the lingual tip, bordering the anterior margin of the lower lobe, is practically normal.

Lower left: In the apex of the lower left there is a definite area of caseous bronchopneumonia. Below the apex, occupying the upper third of the lower lobe, there are abnormal studdings which are probably the result of caseous bronchopneumonia. Calcified areas are noted throughout the lower part of the lower lobe, suggesting calcification at the crotches of the vessels and the bronchi which are probably healed.

Gross pathological description: Pleura appears normal. Immediately posterior to the bronchus is a large caseous and calcareous lymph node measuring 2.5 by 3 cm.

Upper lobe: The lobe shows a heavy involvement of confluent tuberculous caseous bronchopneumonia. The consolidation is heaviest in the areas of the first and second interspace trunks anteriorly with less dense involvement of the same trunks posteriorly. The area of the vertebral trunk is comparatively normal except for some thickening of the walls of the bronchi and a few scattered small areas of caseous bronchopneumonia. Along the main stem bronchus to the lingual tip close to the hilum there is seen a cluster of tubercles and areas of caseous pneumonia about the bronchus, leading to a central area of lesser density which give the suggestion of cavity as seen on the plate. The extreme lingual tip appears normal.

Lower lobe: Shows less involvement. The walls of the bronchi are thickened with some calcification in the main stem bronchus. There is also some dilatation of the bronchi. In the apex is an area of confluent tuberculous caseous bronchopneumonia with some fibrosis. The lower part of the lobe shows only a few scattered studded areas.

Microscopic pathology:

Block 1. Location: Upper lobe, area of first interspace trunk anteriorly.

Reading: Numerous areas of caseous pneumonia with beginning softening of the centre; also interstitial tubercles, and some thickening of septa.

Block 2. Location: Lower portion of area of second interspace trunk anteriorly.

Reading: Numerous areas of tuberculous caseous and gelatinous bronchopneumonia with hemorrhage in periphery of some of them.

Block 3. Location: Apex of upper lobe posteriorly.

Reading: Lung section practically normal. Edema of the septa and perivascular connective tissue. Lymphatics are dilated. One bronchus shows a slight increase of lymphoid cells in its wall.

Block 4. Location: Posterior surface of middle of lower lobe.

Reading: Section shows slight thickening of the pleura and general congestion of the blood vessels. There is one large area of caseous tuberculosis, about 6 mm. from the pleura, and several small areas adjacent to the bronchi at a greater depth in the section. There is one area of acute bronchopneumonia under the pleura.

Block 5. Location: Lingual tip in area suggestive of cavity on the plate.

Reading: Many areas of tuberculous bronchopneumonia, with some interstitial tubercles and marked edema of the perivascular connective tissue.

Block 6. Location: Main stem bronchus to the lower lobe near the hilum.

Reading: Numerous areas of tuberculous bronchopneumonia, edema of the perivascular and peribronchial connective tissue, with some conglomerate tubercles in the lymph node at the hilum.

No. 1199. E. B. Age forty-nine. This case shows the limitations of an X-ray reading. The densities on the right side, caused partially by hemorrhage and acute pneumonia, cannot be definitely read. The even qualities of the densities are not characteristic of tuberculosis. The central tuberculous lesion located by the X-ray in the upper left lobe and verified by the gross pathological reading is interesting.

X-ray Reading: Old scars are noted in the left apex. Just beyond the crotch of one of the trunks, approximately the lower branch of the second interspace trunk, which should be seen behind the third interspace, in a chest plate, is an area which suggests a central tuberculous lesion or infarct. (There is a very slight tuberculous lesion seen near the pleura just beyond this.) On the whole, the markings of this lung are very much interwoven but definite tuberculous lesions are not general. Old scars and diffuse lesions are seen throughout the upper right, except at the vertebral border. The middle and lower right shows abnormal densities which are impossible to read. The markings of this lung are not characteristic of tuberculosis, although the scars in the pleura suggest such an etiology.

Gross pathological description: Lower left lobe has been removed. Pleura is thickened over greater part of both lungs, but especially over the lower right lobe.

Upper left lobe: An adhesion with pleural thickening is found on the apex posteriorly. In the lung in the area of the second interspace trunk posteriorly is found a conglomerate tuberculous mass.

Microscopic pathology:

Block 1. Location: Upper right lobe in area of first interspace trunk.

Reading: Pleura is somewhat thickened and edematous. Extending from the pleura into the lung, along a septum, is a triangular fibrous scar, 8 mm. wide and 4 mm. in depth. The scar is pigmented and also shows some accumulation of lymphoid cells. Deeper in the section there are several areas of acute bronchopneumonia, showing much peripheral hemorrhage with intervening edema of the alveolar spaces.

Block 2. Location: Upper right lobe just above no. 1 in area of vertebral trunk posteriorly.

Reading: Section shows some chronic thickening of the lung framework, with a rather wide connective tissue scar involving the pleura and dipping into the lung. The lung tissue in general shows heavy edema with scattered areas of bronchopneumonia surrounded by areas of hemorrhage. One area of hemorrhage which is roughly quadrilateral measures 1 by 1.5 cm. Lung framework through this hemorrhage is not necrotic.

Block 3. Location: Upper right lobe in anterior area of vertebral trunk.

Reading: Pleura is somewhat thickened and edematous, with some old fibrous adhesions. The lung septa are edematous but not generally thickened. There is some anthracosis with increase connective tissue about it in the septa and lung framework. There is also some emphysema and bronchial dilatation. The bronchi contain a purulent secretion. No tuberculosis is found.

Block 5. Location: Area of second interspace trunk in the upper left lobe.

Reading: Pleura shows a cellular increase and some anthracosis. Lung tissue in general shows slight emphysema and moderate anthracosis. Deeper in the section there are several areas in which the lung framework is thickened. The thickening is apparently due to the presence of lymphocytes and large mononuclears within the lung framework, with some fibroblastic increase. In some of these areas the alveoli show organizing pneumonia. The lymphoid tissue in the neighborhood of the bronchi and vessels is increased in amount. One of these masses of lymphoid tissue shows a distinct conglomerate tubercle.

No. 1124. J. Y. The striking and most interesting point in this case is the "snowstorm-like density" in the lower left lobe, which is due to hemorrhage and acute pneumonia.

X-ray Reading: Plate is spotted. Both upper lobes show heavy tuberculous involvement and extensive cavitation. An area of calcification is seen along the left bronchus. Lower left lobe shows a snowstorm-like density which does not suggest tuberculosis. Lung tissue appears normal in lingual tip of the upper lobe and inferior portion of the lower lobe.

Gross pathological description: Right lung: Upper lobe shows heavy involvement with tuberculous caseous pneumonia and extreme cavitation. Middle and lower lobes are practically all consolidated with tuberculous, caseous pneumonia.

Left lung: Upper lobe shows same condition as upper right with tuberculous caseous pneumonia and old cavities. Lower lobe in apex shows some firmness due to congestion and infiltration. Normal lung tissue is found in the lingual tip of the upper lobe and inferior margin and lower lateral third of the lower lobe. Small calcified area is found lateral to the left bronchus.

Microscopic pathology:

Block 1. Location: Posterior surface of the apex of the lower lobe.

Reading: Pleura is only slightly thickened. Lung tissue shows extreme congestion of all vessels, scattered areas of acute bronchopneumonia with intervening edema and some hemorrhage. No tuberculosis seen in this section.

No. 1218. B. J.

X-ray Reading: All lobes show tuberculous involvement. The oldest tuberculous involvement is found in the upper left lobe. The predominant lesion in this lobe is old fibroid tuberculosis, with extensive cavity formation and much lobular caseation. The lower left lobe shows a large mass of caseous pneumonia involving a large part of the lobe, from the apex to the base along the mesial and posterior borders. Lateral to this is also found extensive caseous pneumonia which, however, is not so dense. A little good lung tissue is found along the anterior and lateral inferior margin of the lobe. The predominant lesion throughout the entire right side is caseous bronchopneumonia with some cavity formation. The entire upper lobe is infiltrated with a flocculent density; except for a narrow strip in the area of the vertebral trunk at the mediastinal surface. This lobe also shows a few small cavities. The middle lobe and upper one-half of the lower lobe show extensive involvement with caseous pneumonia, which, however, is not as dense as on the left side and undoubtedly is more recent. The anterior and mesial portions at the base of the lobe are comparatively normal.

Gross pathological description: Left lung: The upper lobe is extensively excavated by large tuberculous cavities and shows involvement in all parts with tuberculous caseous pneumonia and fibrosis. The lower lobe in general shows the same condition as the upper lobe with less cavitation. The heaviest consolidation is in the apex and posterior portion of the lobe. The anterior inferior margin of the lobe is soft and comparatively normal.

Right lung: Upper and middle lobes both show extensive tuberculous caseous bronchopneumonia in practically all parts. The areas of pneumonia are less confluent and the consolidation is not as uniformly heavy as in the left lung. The upper lobe shows several small cavities. A narrow strip of lung tissue in the area of the vertebral trunk is comparatively free from tuberculosis. Lower lobe in its upper half shows a similar condition to that found in the other lobes without cavitation. The anterior inferior portion of the lobe is comparatively normal.

Microscopic pathology:

Block 1. Location: Posterior inferior margin of the lower right lobe in area showing diffuse coarse mottling.

Reading: Pleura shows fibrous adhesions. Lung tissue shows extreme edema and many areas of caseous and gelatinous bronchopneumonia. Some of the caseous areas join into an area, roughly 2 by 1 cm. Septa are not thickened and the lung framework is practically normal. There is slight anthracosis.

No. 1124. P. M.

X-ray reading: Upper and middle lobes heavily involved with tuberculous caseous pneumonia. Upper lobe honeycombed with thin walled cavities. Lower lobe on posterior surface in the apex shows a fan.

Gross pathological description: Lower lobe: The upper third is practically consolidated with caseous bronchopneumonia. On the posterior surface just below the apex is a definite triangular area of caseous bronchopneumonia, below which is an area of comparatively normal lung tissue. Along the main stem bronchus running to the base are scattered areas of bronchopneumonia, showing less caseation. Along the inferior margin the lung is soft and practically normal. There is some thickening of the walls of the bronchi throughout the lobe.

Upper and middle lobes: Practically consolidated with confluent tuberculous caseous bronchopneumonia. Both lobes show numerous thin walled cavities, especially the upper lobe which is almost entirely destroyed.

Microscopic pathology:

Block 1. Location: Anterior part of upper right lobe, showing peculiar thin walled cavities.

Reading: Pleura shows fibrous thickening. Lymph vessels are dilated. Pleura is closely approached by several areas of tuberculous bronchopneumonia, which show softening and beginning cavity formation in their caseous centres. Similar areas are seen deeper in section. Some fibrous thickening of septa and alveolar framework. No well marked interstitial tubercles. Some tubercles are found in dilated lymphatics.

Block 2. Location: Base of lower right, showing comparatively normal lung tissue.

Reading: Section shows in general normal lung tissue. Two small areas of tuberculous bronchopneumonia are found and one caseous interstitial tubercle, adjacent to which there is thickening of the alveolar walls with organizing exudate in some of the alveoli.

Block 3. Location: Apex of upper right lobe.

Reading: Considerable anthracosis. Marked interstitial sclerosis involving septa and lung framework. Numerous old caseous encapsulated tubercles in septa. Many areas of caseous and gelatinous tuberculous bronchopneumonia.

No. 1128. G. H.

X-ray reading: The entire upper lobe is honeycombed with cavities and is heavily involved throughout in caseous bronchopneumonia. The middle lobe is similarly involved with numerous smaller cavities. The anterior inferior margin just above the incisura shows greatly increased density due to uniform consolidation of caseation. A large calcified area is seen above and internal to the main bronchus. There is another one in the opposite side of the bronchus in the crotch and one further down the bronchus. The lower lobe in its apex shows a similar involvement of caseous bronchopneumonia with cavities. The main stem bronchus is very prominent and small caseous masses are seen along its course to the posterior inferior margin, where there is a density of caseous bronchopneumonia and a small dense mass of solid caseation. The posterior portion of the inferior margin is normal.

Gross pathological description: The upper lobe shows numerous tuberculous cavities of various sizes. The entire lobe is involved with areas of tuberculous caseous bronchopneumonia and small yellow tubercles. The middle lobe is similarly involved with numerous cavities. Along the main bronchus at the hilum are three areas of calcification. The anterior margin, especially at the inferior angle, is heavily consolidated with confluent tuberculous caseous pneumonia. The lower lobe shows the same general condition in its apex with a few cavities. There are several scattered areas of tuberculous caseous pneumonia and yellow tubercles along the main stem bronchus, which is dilated and the walls of which are thickened. The same condition is found at the end of the bronchus at the base. The middle portion of the posterior surface is comparatively normal.

Microscopic pathology:

Block 1. Location: Posterior branch of the main stem bronchus to the lower lobe at the base.

Reading: Pleura is not thickened. Septa are edematous. Lymphatics are dilated. There is seen one large encapsulated softened caseous mass, 3 by 3 mm., which on close examination proves to be a bronchial wall with caseous contents. The muscle fibres are still noncaseated. Between this area and the pleura are several large interstitial conglomerate tubercles with slight surrounding pneumonia. The walls of the smaller bronchi are also involved in a caseasting process.

Block 2. Location: Middle area of diaphragmatic surface of lower lobe.

Reading: There is some calcification of the bronchial cartilages, and general edema of the connective tissue framework. Numerous areas of caseous bronchitis and caseous bronchopneumonia are seen. Some interstitial peribronchial tubercles are present.

2. CASES OF PUERILE TUBERCULOSIS

No. 1202. A. G.

X-ray reading: Eight large and several small calcified areas can be seen at the right hilum. All lobes of both lungs show diffuse disseminated tuberculosis with small cavities in both apices. The pathology is apparently diffuse caseous bronchopneumonia and general miliary tuberculosis. The only normal lung tissue is at the extreme anterior inferior margins of both lower lobes.

Gross pathological description: All lobes of both lungs show a uniform diffuse scattering of small yellowish tubercles and confluent areas of tuberculous caseous pneumonia. There is softening and a few small cavities in the apices of both upper lobes. All lobes are practically uniformly consolidated. The only comparatively normal lung tissue is found at the anterior inferior margin of both lower lobes.

Microscopic pathology:

Block 1. Location: Lateral surface of the middle third of the lower left lobe.

Reading: Pleura shows anthracosis and vascular dilatation. Section in general shows numerous areas of caseous and gelatinous pneumonia with intervening edema. There are also numerous interstitial miliary and conglomerate tubercles lying in the peribronchial tissue and in the septa.

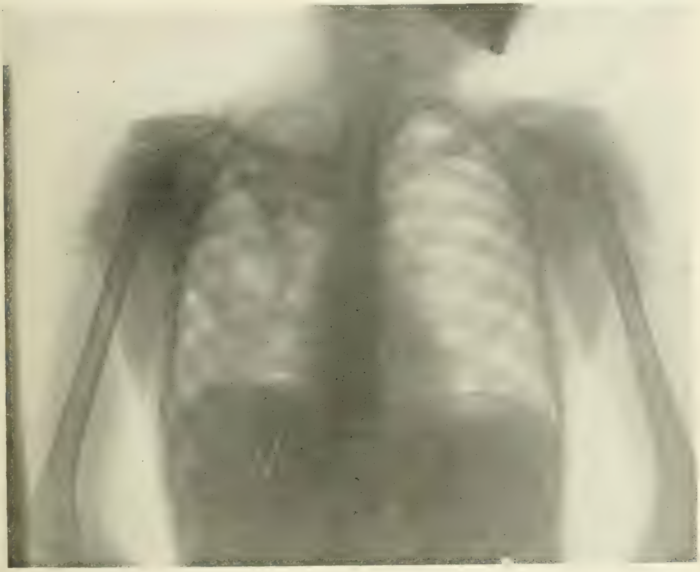

FIG. 11. No. 1168. X-RAY CHEST PLATE, FOUR MONTHS BEFORE DEATH

A mass of increased density involves the vertebral and the first interspace trunks of the upper right. Within this density are areas of lesser density which suggest cavities, connected to the bronchus within a mass of pneumonia which is probably tuberculous. There is a haziness throughout the remaining portion of the right lung, including the second interspace trunks of the upper right and the middle and lower right lobes. This suggests gelatinous pneumonia due to tuberculosis.

Left lung: A delicate fan is noted in the left apex which is probably due to the same etiology. The remaining portion of the left lung is clear.

The prognosis is desperate on account of the caseous and gelatinous pneumonia involving the entire right side, in a child of eight years. Unless etiology other than tuberculosis can be substantiated, this prognosis must stand.

Note: Such a lesion in an older patient must be differentiated from syphilis.

No. 1168. G. W. Age eight. Colored. (See fig. 11 for X-ray plates of chest.)

X-ray reading of lung plate (see fig. 12): Posterior surface to plate. Entire upper right lobe is heavily involved with tuberculous pneumonia and destroyed by cavities. Middle and lower right lobes are also badly involved by the same tuberculous condition. On the left side are found curious cone-shaped densities throughout the upper lobe and apex of the lower lobe. One triangular density is found below a pleural scar on the lateral border of the upper lobe just above the incisura. Anterior surface of upper lobe near the vertebral margin shows a density of irregular shape.

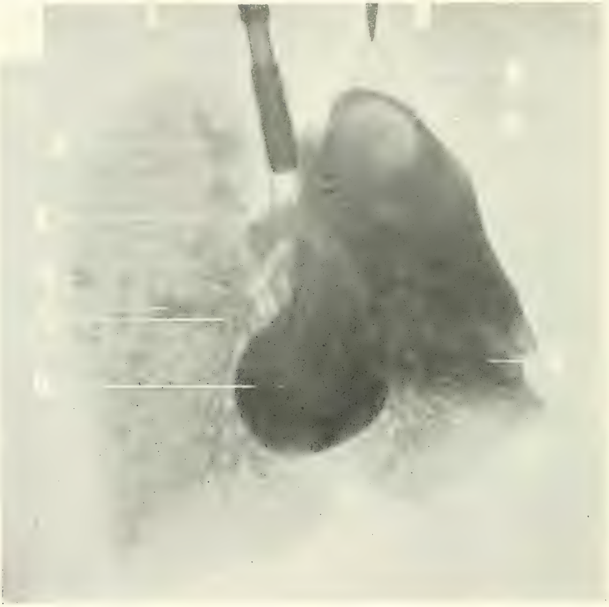

FIG. 12. NO. 1168. X-RAY LUNG PLATE

A—Cavity. *B*—Area of caseous bronchopneumonia. *C*—Area of caseous bronchopneumonia. *D*—Pleural adhesion. *E*—Arch of aorta passing over left bronchus. *F*—Middle lobe *G*—Heart. *3*, *4*, and *5*—Areas of respective blocks.

Note: These lesions, in a child of eight, are an example of the puerile type of tuberculous infection, suggesting little resistance. The lymph nodes are greatly involved and there is massive destruction of lung by heavy caseation with little sign of fibrosis. The densities in the left lung are very curious and apart from the lesions on the right side could not be read as tuberculous. The density of block 4 produced by caseous pneumonia is identical with the density which might result from an infarct.

The lesions in the left lung are sometimes spoken of as circular, central or globular lesions.

Gross pathological description: Right lung: The pleura over the entire lung is thickened, but especially at the apex, with numerous adhesions. All the lobes are bound together by very firm fibrous adhesions in the incisurae. The bifurcation and right paratracheal lymph nodes are very large and caseous. All the lobes are massively consolidated with confluent caseous pneumonia and riddled with cavities. The entire apex of the upper lobe is occupied by a cavity, measuring 4 by 5 cm., the next largest cavity being found in the apex of the lower lobe and measures 3 by 4 cm. In the base of the upper lobe is found a large cavity which has broken through the pleural layers in the incisura into the middle lobe. The walls of the bronchi are markedly thickened in all parts of the lung and in the lower lobe the bronchi are in several places greatly dilated. The only air bearing tissue in the entire lung is along the inferior margin of the lower lobe and the anterior margin of the middle lobe.

Left lung: The upper lobe is soft and air bearing throughout its greatest extent, but scattered through it are several isolated areas of caseous bronchopneumonia. The largest of these areas are found on the vertebral trunk, on the lateral surface immediately under the pleura in the area of the second interspace trunk, and just below the area of the same trunk near the hilum. The lingual tip also shows a few scattered smaller areas of caseous bronchopneumonia. The lower lobe shows a picture much the same as that of the upper lobe. The areas of caseous bronchopneumonia are fewer and smaller; most of them are found in the apex. The walls of the bronchi are somewhat thickened.

Microscopic pathology:

Block 1. Location: Lymph node from hilum of right lung.

Reading: Lymph node shows anthracosis, hemorrhage, miliary and conglomerate tubercles.

Block 2. Location: Lymph node from hilum of left lung.

Reading: Lymph node very similar to block 1 showing, however, larger tuberculous masses.

Block 3. Location: Lateral surface of upper lobe just above the incisura.

Reading: Lung in general normal, one small area of tuberculous caseous bronchopneumonia.

Block 4. Location: Lateral surface of upper lobe just above block 3 in triangular density seen on plate.

Reading: Large areas of tuberculous caseous bronchopneumonia; one occupying apparently the whole of a secondary lobule with base on the pleura (see fig. 13).

Block 5. Location: Upper border of cardiac notch.

Reading: Thickened pleura and septa. Tuberculous caseous pneumonia close to pleura on both sides of septa.

No. 1256. E. S.

X-ray reading of lung plate (see fig. 14): Diffuse miliary tuberculosis; all lobes involved, but most marked in apex of upper right lobe. Calcification is seen to the right side of the trachea at the carina and at the bifurcation of the bronchi going to both upper lobes. A calcified nodule is seen in the upper right lobe near a scar below the lateral surface in an area mapped out as the first interspace. A small area of calcification is also seen in the upper left zone along one of the posterior branches of the second interspace trunks. A small cavity is seen in lingual tip.

Gross pathological description: The pleura over both lungs appears normal. On the right side of the trachea immediately at the bifurcation is found a heavily calcified lymph node measuring 2.5 by 3 cm.

Right lung: upper lobe: In the area of the first interspace trunk on the lateral surface, 1 cm. under the pleura, is found a calcified nodule, measuring 1.5 by 0.5 cm., surrounded immediately by emphysema and some radiating fibrosis. The entire lobe feels soft and is air containing but on section there is seen to be an even generalized scattering in all parts of minute white tubercles.

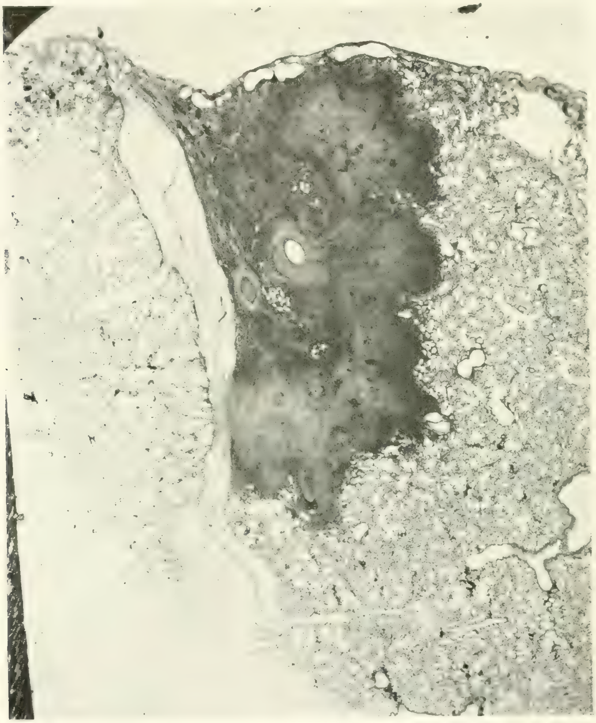

FIG. 13. NO. 1168. MICROSCOPIC SECTION THROUGH BLOCK 4

Middle and lower lobes: show exactly the same generalized scattering of minute white tubercles.

Left lung: upper lobe: Immediately above the main bronchus to the upper lobe at the hilum is found an old caseous lymph node (C) with some ca'careous infiltration, measuring 2.5 by 3 cm. In the lingual tip immediate to the main stem bronchus, but not connecting with it, is a small cavity (D), 1.5 by 1.5 cm., containing a white cheesy material. The rest of the lobe shows the same generalized scattering of minute white tubercles as in the right lung. Lower lobe: Shows exactly the same general condition as all the other lobes.

Microscopic pathology:

Block 2. Location: Right apex below the notch for the subclavian artery.

Reading: Pleura slightly involved. Many areas of tubercles surrounded by a slight border of pneumonia. On edge of section there is an irregular patch of pneumonia in which the exudate is largely polymorphonuclear leucocytes and which shows no caseation. (See fig. 15.)

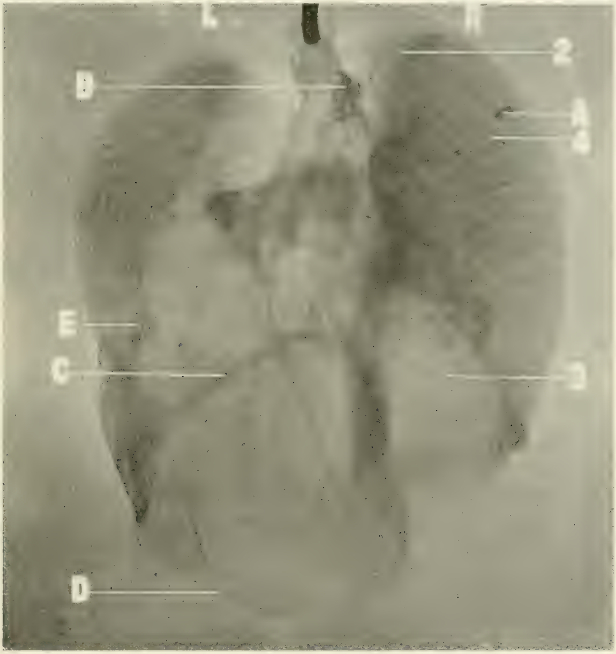

Fig. 14. No. 1256. X-Ray Plate of Lung; Heart Removed

A—Calcified area under pleural scar. *B*—Calcified lymph nodes. *C*—Anterior basal margin. *D*—Posterior basal margin. *E*—Cavity in lingual tip. *2, 3, 4*—Areas of respective blocks.

Block 3. Location: Base of lower right lobe.

Reading: Dilatation of lymphatics in pleura and septa. Increase in the connective tissue cells of the pleura. Some increase in lymphocytes in framework, especially about the blood vessels. Deeper in the section there are a few caseous tubercles surrounded by slight tuberculous pneumonia. The bronchi show a purulent content and a lymphocytic infiltration of their walls.

Block 4. Location: Area of second interspace trunk of upper right lobe.

Reading: Edema and hemorrhage in the pleura. Increase in connective tissue cells and lymphocytes in the pleura. Marked dilatation of the lymphatics in the pleura and septa, with considerable number of lymphocytes and phagocytes in the septal lymphatics. The lung framework is irregularly thickened by increase in connective tissue cells and by infiltration of lymphocytes and large mononuclear elements. A few alveoli contain mononuclear phagocytes, some lymphocytes and a few polymorphonuclear leucocytes. Anthracosis is relatively slight. No absolutely definite tuberculous lesion is found.

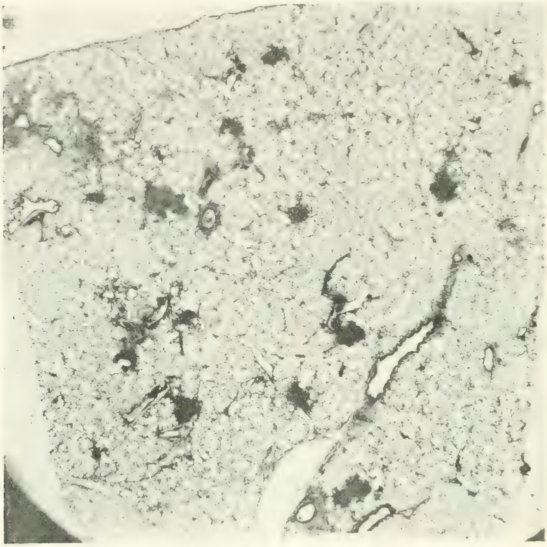

FIG. 15. NO. 1256. MICROSCOPIC SECTION THROUGH BLOCK 2

No. 1095. M. J. Colored.

X-ray reading of lung plates (see fig. 16): *Right lung:* A large mass of calcareous material is noted at the right hilum, just above and anterior to the eparterial bronchus. The trunks to the upper lobe are heavy, but the linear markings are not involved except for some studding along the linear markings of the posterior branches of the first and second interspace trunks. The middle and lower lobes cannot be definitely separated. The linear markings of what are probably the middle lobe trunks show some increased density with one or two spots of calcification. A similar area is seen in the lower part of the upper third of the lower lobe. In the lower lobe, along the posterior surface, near the inferior margin, there is an area of increased density suggesting caseous bronchopneumonia. Abnormal densities are noted along the main stem bronchus and the main branch of the main stem bronchus going to the middle and lower lobes.

Left lung: It is impossible to make out definitely the lobes on the left side because, first, the trunks cannot be made out on account of the general increased density extending from the apex to the base throughout all lobes and, secondly, the peripheral shadows suggest more than two lobes. The densities on the left side are undoubtedly due to caseation, but they are seen indistinctly, as though one were looking through a snowstorm. Undoubtedly they are the result of caseous pneumonia, but why the snowstorm effect must be determined.

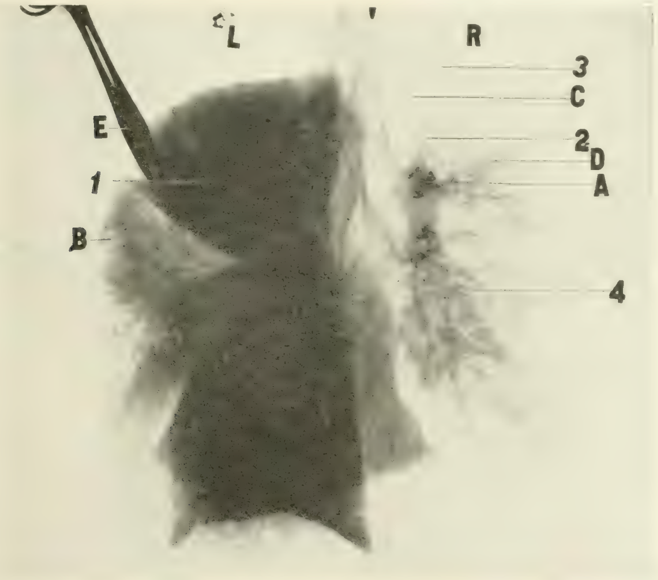

Fig. 16. No. 1095. X-Ray Plate of Lung

Heart removed. Abnormal lobation with three lobes on the left side.

A—Caseocalcareous lymph nodes. *B*—Cavities. *C*—Vertebral trunk. *D*—Second interspace trunk. *E*—Forceps used to support the lung. *1, 2, 3, 4*—Areas of respective blocks.

Diagnosis: Caseous pneumonia throughout the lobes on the left side. The exact character of the pneumonia is not determined. Tuberculous lesions throughout the right side. Peribronchial tuberculosis noted in the upper lobe with a little caseous bronchopneumonia in the lower part of the upper lobe. Old caseous bronchopneumonia in the middle and in the upper third of the lower right and more recent caseous bronchopneumonia near the posterior margin of the lower right.

Note: The most striking feature of this pair of lungs is that no definite apical or adult tuberculosis is made out. The lesions are comparatively small on the right side and are very extensive throughout the left. The lesions on the left are caseous from apex to base. Such a distribution suggests peurile tuberculosis with a desperate prognosis or tuberculosis complicated with some other lesion such as syphilis.

Gross pathological description: Left lung: Three lobes are found on this side. *Upper lobe:* is entirely uniformly consolidated with heavy tuberculous caseous pneumonia. *Middle lobe:* also shows heavy involvement with the same pneumonic process but the consolidation is less homogeneous and dense. There are several cavities in the upper portion of the lobe. The lower portion of the lobe shows some comparatively normal air bearing lung tissue. *Lower lobe:* in its greatest extent shows the same heavy consolidation with tuberculous caseous pneumonia. A small amount of comparatively normal soft lung tissue is found at the inferior margin.

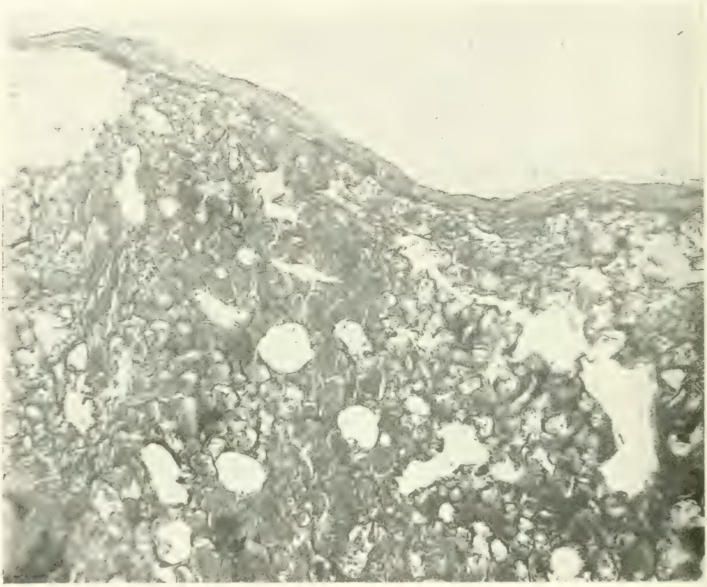

FIG. 17. NO. 1095. MICROSCOPIC SECTION THROUGH BLOCK 1

Right lung: In the *upper lobe* just above the eparterial bronchus is found a large mass of calcified caseous lymph nodes. Except for some thickening of the walls of the bronchi the lung tissue appears normal. The *middle lobe* presents the same picture as the upper lobe. The *lower lobe* has the same general appearance as the other two lobes with extensive fibrosis at the hilum. In the lower portion of the lobe are found a few rather firm areas suggestive of the exudation of bronchopneumonia.

Microscopic pathology:

Block 1. Location: Upper left lobe showing deep homogeneous density.

Reading: Section shows tuberculous pseudolobar gelatinous and early caseous pneumonia. There is moderate anthracosis. Pleura shows thickening with diffuse infiltration with lymphocytes and dilatation of the vessels (see fig. 17).

Block 2. Location: Upper right lobe in area between first and second interspace trunks.

Reading: Section shows normal lung tissue except for anthracosis and mucopurulent bronchial secretion. There are some calcified cartilages in the walls of the bronchi.

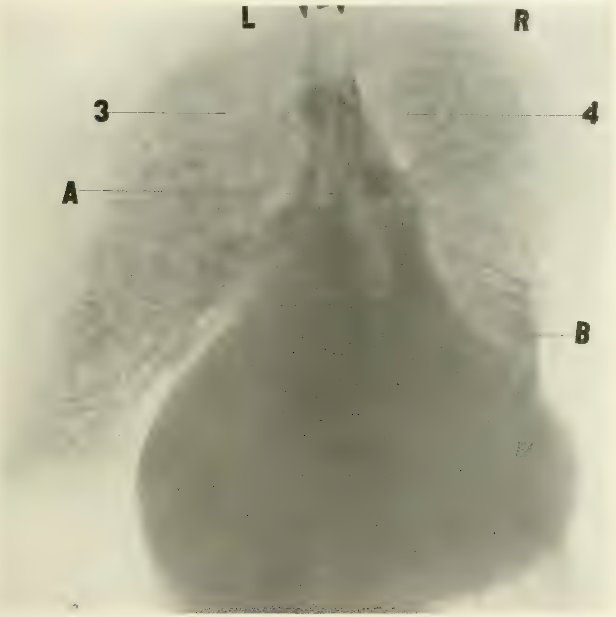

FIG. 18. NO. 1063. X-RAY PLATE OF LUNG

Heart intact; pericardial effusion.
A—Carina. *B*—Compressed lower right lobe. *3; 4*—Areas of respective blocks.

Block 3. Location: Apex of upper right in area appearing comparatively normal. Vertebral trunk.

Reading: Section is in general normal except for anthracosis and mucopurulent bronchial secretion. About one small bronchus the alveoli are filled with exudate, consisting of fibrin, serum, large and small mononuclear cells, with few polymorphonuclear leucocytes. There is beginning caseation.

Block 4. Location: Apex of lower right lobe.

Reading: There are several areas in which the smaller bronchi show loss of epithelium and infiltration of the walls with lymphocytes. These are surrounded by small areas of pneumonia. At the edge of the section is one quite extensive area of tuberculous gelatinous and caseous pneumonia.

No. 1063. A. B. This case is an example of a general miliary tuberculosis to which is added diffuse disseminated caseous bronchopneumonia.

X-ray reading of lung plates taken October 15, 1916 (see fig. 18): Marked pericardial effusion. General miliary tuberculosis with diffuse disseminated, caseous bronchopneumonia

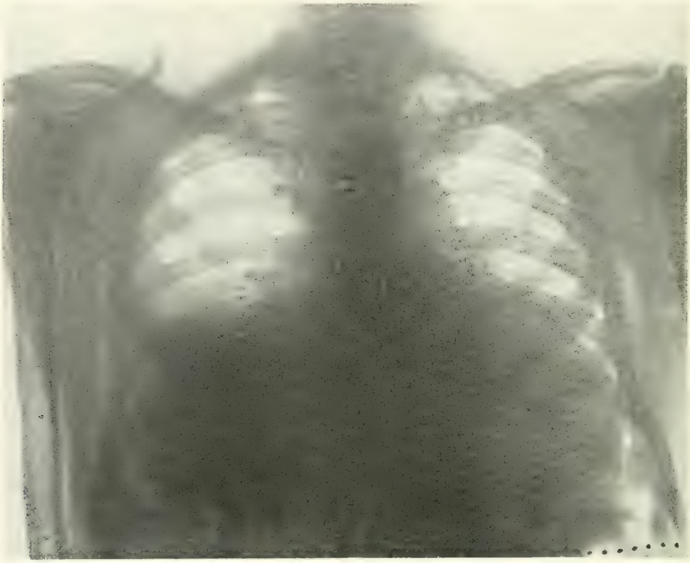

FIG. 19. No. 1063. X-RAY CHEST PLATES TAKEN SEPTEMBER 7, 1916, ONE MONTH BEFORE DEATH

Definite tuberculous lesions are noted in both apices and in the first interspace trunks of the upper right. The abnormal density about the heart and the right base density might be the result of tuberuclosis or compression. The pericardial effusion obscures the entire left base. An abnormal density obscures the right base. This is probably the result of fluid, because the surface of this density is definitely concave; but the right base is contracted and the effusion may be organized. The contraction is in contrast to the distention at the left base.

Note: The general fibrosis, anthracosis and miliary tuberculosis found upon section and seen in the X-ray of the lungs cannot be made out from these plates or in plates taken two months before death.

Postmortem examination shows much fluid in pleural and pericardial cavities.

throughout both lungs. Thickening of the pleura over the right lung. The incisura below the upper right lobe is abnormally heavy. (See fig. 19 for X-ray plate of chest.)

Gross pathological description: All lobes of both lungs show a general diffuse scattering of caseous nodules and areas of tuberculous caseous bronchopneumonia. There is also some general thickening of the walls of the bronchi and septa. Caseous lymph nodes with some calcification are found at the hilum of both lungs.

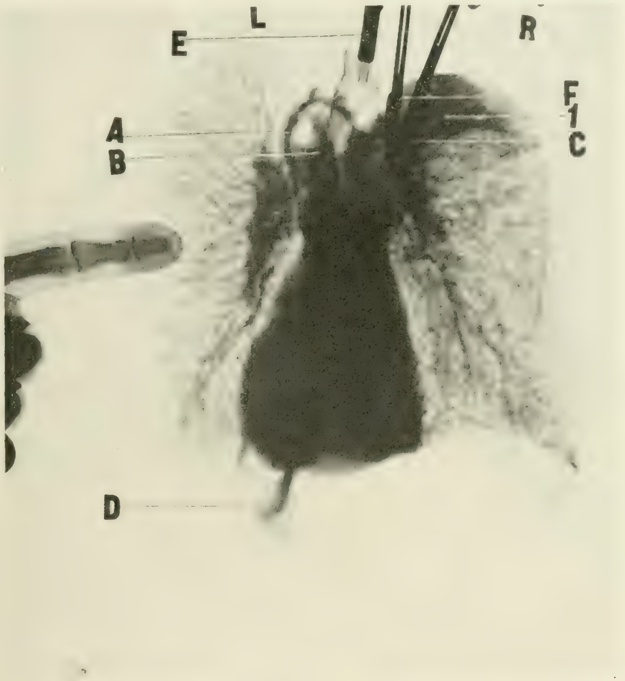

Fig. 20. No. 1147. X-Ray Plate of Lung; Heart Intact

A—Arch of aorta showing calcification. *B*—Calcified cartilages in trachea and bronchi. *C*—Carina with neighboring calcified lymph nodes. *D*—Pericardial shreds. *E*—Tube used for inflation. *F*—Forceps used to close tears in pleura. *1*—Area of block.

Microscopic pathology:

Block 1. Location: Lymph node at the hilum.

Reading: The lymph node shows anthracosis and many miliary and conglomerate tubercles with slight caseation.

Block 2. Location: Lymph node at the hilum.

Reading: Many caseous conglomerate tubercles with some calcium infiltration.

Block 3. Location: Upper left lobe in area of first interspace trunk.

Reading: Marked anthracosis. The pleura and septa show fibrous thickening. Numerous caseous conglomerate tubercles are found in the septa. There are many small tubercles scattered in the alveolar walls. The walls of the bronchi show caseation and contain exudate. Some peribronchial tubercles are seen.

Block 4. Location: Upper right lobe in area of first interspace trunk showing a fan.

Reading: The pleura is thickened, edematous and congested with some organizing fibrinous exudate on its surface. Extending from the pleura into the lung is a heavily pigmented dense fibrous triangle with base on the pleura. Below this and practically continuous with it, is an encapsulated area of caseous pneumonia which is beginning to soften at its centre. About this are many recent miliary and conglomerate tubercles and some older interstitial caseous tuberculous masses. There is thickening of the alveolar framework in the vicinity of these masses.

3. CASES WITH NONTUBERCULOUS LESIONS

No. 1147. R. S. Age sixty-nine. The striking feature of this case is the single definite lesion in the right apex, the pathology of which cannot be read. It illustrates a limitation of the X-ray.

Chest plate reading: Very slight lesions are noted in the vertebral trunk of the upper left lobe. A definite fan is seen on the vertebral and first interspace trunks of the upper right lobe. Neither of these densities are characteristic of tuberculosis.

X-ray reading of lung plate (see fig. 20): Plates overexposed. Back of lungs to plate. A lesion is present in the upper right lobe near the vertebral margin. Linear markings throughout the remainder of both lungs are heavy and somewhat interwoven, but do not suggest tuberculosis. There is considerable calcification of the cartilages in the walls of the bronchi and also within the lymph nodes at the hilum. If calcification denotes tuberculosis the latter is present; otherwise it is not suggested, except in apex of upper right lobe which is indefinite.

Gross pathological description: Left lung: Pleura over the upper lobe and apex of the lower lobe shows several areas of fibrous thickening and some adhesions. The lymph nodes at the hilum are large and caseated with some calcification in the nodes and walls of the bronchi. *Upper lobe:* The apex has an increased firmness as of some fibrosis, but the entire lobe is air containing and shows no gross tuberculous lesion. The bronchi are dilated and there is some thickening of their walls as well as those of the vessels. *Lower lobe:* Is soft and appears normal throughout except for some thickening of the walls of the vessels and bronchi, which are dilated.

Right lung: The apex of the upper lobe is markedly foreshortened and contracted by a broad fibrous scar extending from the pleura into the lung for a distance of 2 cm. The lung tissue surrounding the scar is contracted due to fibrous bands radiating out from the firm area. The scar is heavily pigmented and very firm, suggesting atelectasis or an old caseous fibrous scar of a latent tuberculous lesion. In the rest of the lobe the walls of the bronchi are thickened and at the hilum show some calcification.

The middle and lower lobes appear normal except for a fibrotic thickening of the walls of the bronchi and the septa.

Microscopic pathology:

Block 1. Location: Apex of right upper lobe.

Reading: Anthracosis well marked; marked induration of lung extending from the pleura for a distance of about 1 cm. into the lung tissue. There are no definite tubercles in the older connective tissue. Some areas show a recent caseation of the tissue. Bronchi lying in this tissue and extending into it from the inner side are dilated, have caseous walls and show a cellular content. Some edema of the alveoli. Chronic fibrous thickening of the pleura. Some congestion and hemorrhage in the pleura. Moderate fibrous thickening of the septa with some thickening of adjacent alveolar walls. Bronchi show purulent exudate with marked desquamation of epithelium. There is heavy lymphocytic infiltration of the bronchial walls with cellular increase in walls of alveoli. The lymphatics of pleura and one septum in particular are heavily filled with large mononuclear phagocytes. No absolute tuberculous lesion is found (see fig. 21).

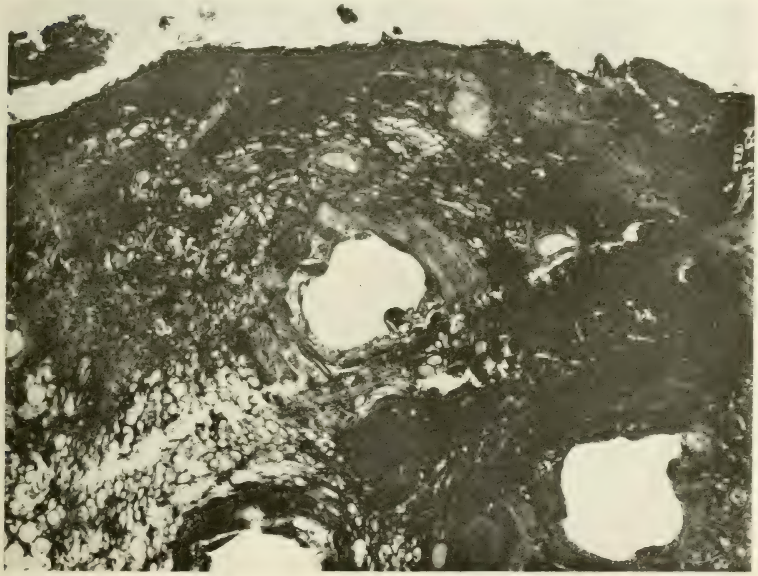

Fig. 21. No. 1147. Microscopic Section through Block 1

Block 3. Location: Apex of left upper lobe.

Reading: Pleura shows slight sclerosis in patches; some fibrous thickening of septa and lung framework, with considerable anthracosis in the lung framework. One heavy area of sclerosis extends from the pleura into the lung with radiating strands extending between the alveoli. This connective tissue shows marked infiltration of mononuclears in several areas. The bronchi, which are dilated, contain a purulent secretion and show a lymphocytic infiltration of their walls. There is no absolute evidence of tuberculosis.

Block 4. Location: Midportion of upper left lobe.

Reading: Except for anthracosis and small area of sclerosis about the pigment the lung tissue appears normal.

No. 1157. J. W. Age fifty-nine. The interesting points in this case are the aneurysm and the density in the middle and apex of the lower lobe. This density of a homogeneous, "snowstorm"-like quality might be the result of hemorrhage or pneumonia. Microscopic section shows it to be due to acute pneumonia.

Reading of X-ray plate of lung (see fig. 22): Back of lung to plate. A large aneursym is made out just above the left bronchus compressing the left upper lobe. The entire upper left is blotted out by a large mass of increased density which suggests a "snowstorm" appearance around the edges. A similar condition is seen in the lower left. This is not so dense and does not occupy the entire lobe. A definite triangular snowstorm density is seen in the posterior part of this lobe, extending from the hilum to the base. It is impossible to determine whether these are the result of hemorrhage or pneumonia.

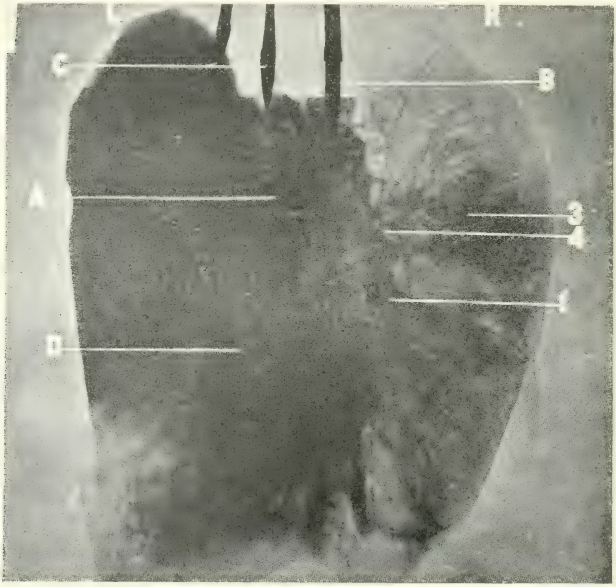

FIG. 22. NO. 1157. X-RAY PLATE OF LUNG; HEART INTACT

A—Aneurysm of arch of aorta overlying the left bronchus. *B*—Tube used for inflation. *C*—Upper forceps used to support the lung. *D*—Lower forceps used to close a tear in the pleura. *1, 3, 4*—areas of respective blocks.

Right lung: The linear markings of the vertebral and the upper branches of the first interspace trunks are clear; but the posterior branches of the second interspace trunks are occupied by a large fan of homogeneous density which does not suggest tuberculosis, but might be the result of hemorrhage or pneumonia. Immediately behind the middle lobe, and possibly within it, there is a large triangular area of increased density involving the main stem bronchus and reaching the pleura posteriorly in the apex of the lower lobe. It is impossible to determine whether this is the result of hemorrhage or pneumonia. In the lower part of the lower right, at the junction of the diaphragmatic anterior margins, is a small area of increased density which suggests acute pneumonia.

Note: As the lesions within the right lung were definitely proved to be pneumonia, it is interesting to note that the right apex is unusually clear and to compare these pneumonic lesions with similar lesions due to hemorrhage.

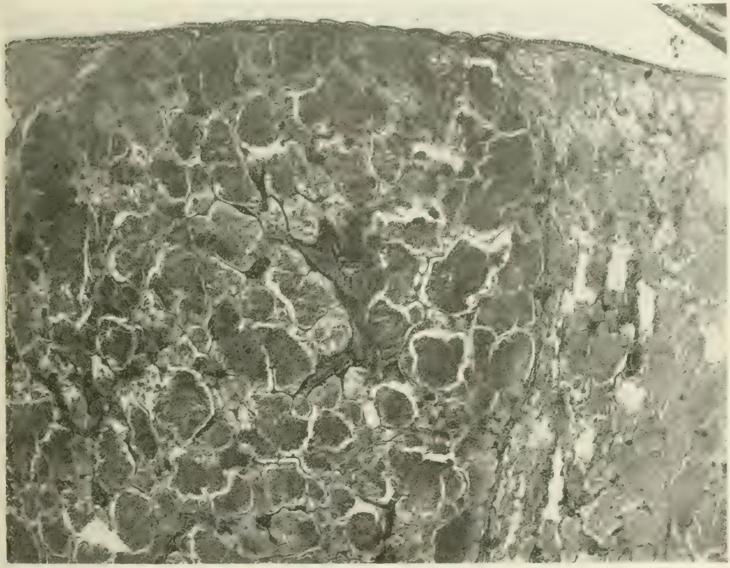

FIG 23. No. 1157. MICROSCOPIC SECTION THROUGH BLOCK 1

Gross pathological description: The arch of the aorta presents a large aneursym which pushes into the hilum of the upper lobe of the left lung to a point within 2 cm. of the anterior margin and 5 cm. of the apex, causing marked compression of the lung tissue of the entire lobe. The aneurysm is filled with a laminated clot and thrombus and shows a constricted opening. In the posterior wall of the aneurysmal sac is found a rupture, 6 mm. in diameter, with hemorrhage into the apex and posterior part of that lobe of the lung.

Microscopic pathology:

Block 1. Location: Apex of lower right lobe.

Reading: Section shows practically uniform consolidation, the alveoli being densely packed with cellular exudate of an acute pneumonia. The vessels of the lung framework are congested. There is no caseation and no tuberculous lesion is found (see fig. 23).

Block 3. Location: Upper right lobe in area of second interspace trunk.

Reading: Section shows some peripheral edema of the lung. Moderate anthracosis and emphysema. There are numerous small patches of acute bronchopneumonia with considerable neighboring edema. The lymphatics of the pleura are dilated with cellular exudate.

Block 4. Location: Same trunk as block 3 but close to hilum.

Reading: Section is through a large bronchus. Close to the bronchus the alveoli are occupied by an acute exudate. The lymphatics are dilated and there is some edema adjacent to the bronchus. No tuberculosis found.

No. 1096. R. S. This case is especially reliable to show nontuberculous densities. The densities in the lower left lobe due to infarcts are interesting to compare with the density which might be produced by caseous pneumonia as in case 1168, G. W. The absence of any apical lesion and the fact that the densities grow progressively heavier from above down, would make it seem most probable that the condition was not tuberculous.

X-ray reading of lung plate (see fig. 24): Back toward the plate. Upper right side is most involved. Masses around eparterial bronchus which suggest glands containing practically no calcification except very near the bronchial wall. Around the main stem bronchus of the lower right lobe are calcified areas which appear to be in the surrounding lung. Bronchus on the left side is comparatvely clear but the trunks of the upper lobe are heavy and capped. The posterior left apical bronchus is studded and apparently reaches the posterior surface. There is an unusual density at the anterior margin of the base of the left upper lobe which involves the lingual tip and the posterior basal margin of the lower lobe. Another area of similar density is seen at the base of this lobe on diaphragmatic surface. On the right side in the upper lobe delicate fans are seen in the vertebral, first and second interspace trunks. These involve mostly the lateral and posterior surfaces. Many diffuse fans are seen in the lower right lobes. Densities grow progressively heavier from above downward. Areas of blocks 1, 2 and 3 along the first interspace trunk of the upper left lobe suggest peribronchial and perivascular inflammation with small areas of calcification along the bronchus. One trunk is distinctly capped. Linear markings are heavy, interwoven and do not reach the periphery. The picture is a typical example of so called "peribronchial" and "perivascular" tuberculosis which we maintain cannot be definitely diagnosed from the X-ray plate. Such increased densities barring calcification may be due to other etiology than tuberculosis.

Gross pathological description: Right lung: The lymph nodes at the hilum are slightly enlarged and heavily anthracotic. There is very considerable fibrosis and thickening ofthe walls of the large bronchi and vessels at the hilum with some calcification in the walls of the bronchi. *Upper lobe:* The lung tissue in general is soft and air bearing. There is considerable thickening of the walls of the bromchi and septa of the lung with slight dilatation of the bronchi. There are also some scattered areas of firmness, suggesting infiltration and pneumonia exudation as bronchopneumonia, especially in the areas of first and second interspace trunks. *Middle lobe* is abortive. *Lower lobe* shows the same general condition as the other lobes with larger areas of bronchopneumonia, especially at the base. There is considerable congestion and some hemorrhage.

Left lung: Lymph nodes at hilum show considerable pigment. Bronchial walls are thickened with some calcification. *Upper lobe* shows the same thickening of the walls of the bronchi and septa as in the right lung. There are a few scattered areas of pneumonic exudate. The extreme lingual tip is firm with infiltration and shows a peculiar honeycombed condition with bronchiectatic cavities. Some of this may be an artefact due to improper inflation. A few minute white areas are also seen, but no definite tuberculosis can be grossly made out. *Lower lobe* has the same general appearance as the other lobes with thickened septa and bronchial walls. There is considerable congestion, some hemorrhage, and a few areas of bronchopneumonia. On the inferior margin, bordering on the diaphragmatic and lateral surfaces immediately under and in the pleura, is a round depressed white firm area (1.5 by 2 cm.) surrounded by hemorrhage, the lesion suggesting an old infarct. On the posterior surface and on a higher level is another similar area which is larger.

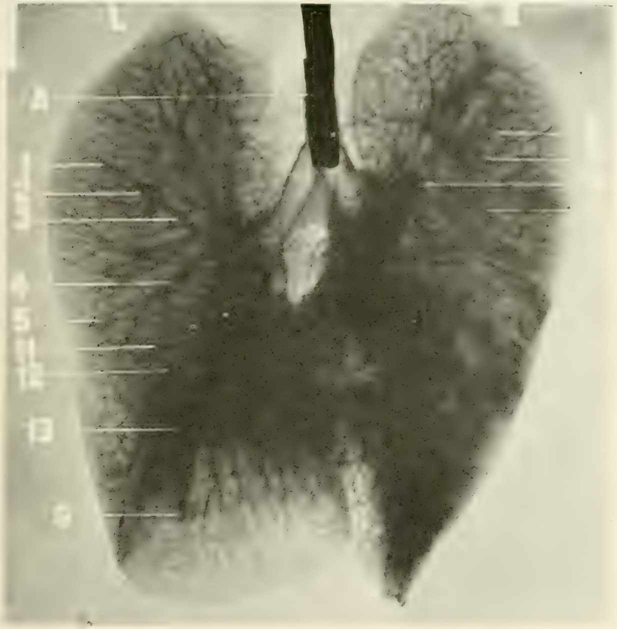

FIG. 24. NO. 1096. X-RAY PLATE OF LUNG

Illustrates heavy trunks, "peribronchial thickening" most marked in the upper left lobe, without tuberculosis.

A—Tube used to inflate the lungs. *1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13*—Areas of respective blocks.

Microscopic pathology:

Block 1. Location: Upper left lobe in peripheral area of first interspace trunk.

Reading: Lung section is in general comparatively normal. A large bronchus shows some calcification of its wall. Between the bronchus and the artery is a comparatively large amount of coal pigment, surrounded by connective tissue. The lymphatics in the septa are dilated. There is slight edema of the alveolar spaces, and the alveolar walls are thin, apparently due to some emphysema. There is some purulent secretion in the bronchi, and adjacent to a small bronchus a few alveoli show an exudate of polymorphonuclear leucocytes. There are also signs of bronchial dilatation.

Block 2. Location: Same trunk as block 1, only nearer the hilum.

Reading: Quite similar to block 1. No tuberculosis found.

Block 3. Location: Same trunk as blocks 1 and 2, only nearer the hilum.

Reading: Section is very similar to preceding ones. There is more marked involvement of the smaller bronchi and of adjacent alveoli by acute exudate.

Block 4. Location: Upper left lobe in area of second interspace trunk at point of greatest density.

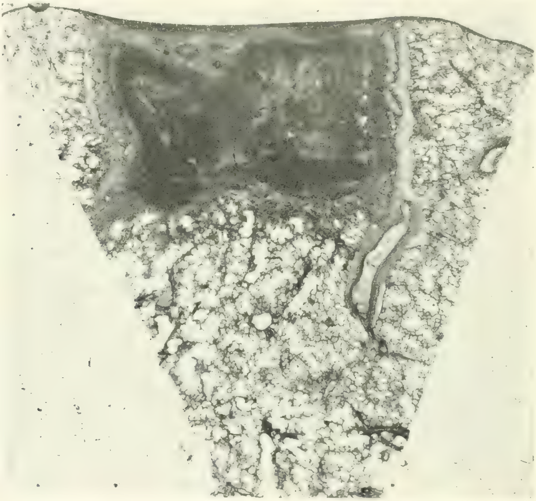

FIG. 25. NO. 1096. MICROSCOPIC SECTION THROUGH BLOCK 6

Reading: Well marked calcification of bronchial cartilages; edema of the perivascular and peribronchial connective tissue. Some dilatation of the lymphatics and some anthracosis. Slight pulmonary edema. No tuberculosis. One lymphatic shows a valve.

Block 5. Location: Second interspace trunk, peripheral to block 4.

Reading: Pleura is not thickened but appears densely fibrous with some anthracosis. Septa are somewhat thickened by fibrous tissue. There is moderate anthracosis and slight emphysena. No tuberculosis.

Block 6. Location: Base of lower left lobe.

Reading: Section is in general similar to the previous sections but shows however a more or less wedged shaped area with base on the pleura, in which there is necrosis of lung framework and alveoli are filled with red blood cells. The area has been invaded by a heavy line of leucocytes which are fragmented and necrotic. *Histological diagnosis:* Old hemorrhagic infarct (see fig. 25).

Block 7. Location: Area of second interspace trunk in upper right lobe showing a delicate fan.

Reading: Section shows numerous areas of acute bronchopneumonia, the alveoli being filled with polymorphonuclear leucocytes without caseation and without tubercle formation.

Block 8. Location: Upper right lobe immediately above block 7, showing a fan.

Reading: Areas of acute bronchopneumonia as in block 7. No tuberculosis.

Block 9. Location: Extension of block 8 toward the hilum.

Reading: Large bronchi are dilated with slight calcification of the cartilages. There is some purulent exudate, edema of the perivascular and peribronchial tissue. Small area of acute pneumonia.

Block 10. Location: Extension of block 9 toward the hilum.

Reading: Large bronchi and vessels are quite similar to block 9. There are also patches of acute pneumonia. The lymph node at the hilum shows well marked anthracosis but is free from tubercles.

Block 11. Location: Lingual tip of left upper lobe.

Reading: Pleura is thickened and shows dilatation and congestion of its blood vessels. The lung framework is markedly thickened throughout the section. The blood vessels are dilated and engorged. The bronchi are enormously dilated, one of them immediately under the pleura measuring 3 mm. across. The walls of the bronchi are thickened and the mucosa is desquamated. Surrounding several of the large bronchi are areas of lung tissue showing thickened alveolar walls and heavy acute exudation of bronchopneumonia. The cartilages in the walls of the bronchi show calcification. No tuberculosis is found.

Block 12. Location. Lingual tip of left upper lobe.

Reading: Section is in general similar to block 11 showing thickened pleura, dilated and congested blood vessels, thickening of lung framework and alveolar walls, marked bronchiectasis, calcification of bronchial cartilages and patches of acute bronchopneumonia.

Block 13. Location: Middle of posterior surface of left lower lobe.

Reading: Pleura is thickened and markedly congested. Immediately under the pleura is an irregularly shaped area with base on the pleura showing necrosis of lung framework, heavy infiltration of polymorphonuclear leucocytes and a border of hemorrhage. On the border of this area the blood vessels are engorged and there are signs of organization. *Histological diagnosis:* Hemorrhagic infarct.

CONCLUSIONS

This study of abnormal lung densities has been limited largely to normal and tuberculous lung tissue. Further studies are necessary and hold great promise. Normal lung tissue can be detected with accuracy so far as our experience has been able to determine.

The ease of detecting abnormal densities within the lung is due to the slight densities cast by normal lung structures.

"Peribronchial and perivascular thickening" does not always mean "peribronchial or perivascular tuberculosis." We have never found it associated with tuberculosis in an adult unless accompanied with fans toward the periphery. By this we do not imply that it may not be associated but that the fact that we have never found it disproves its diagnostic value.

The great value of X-ray study is that it can be used during the life of the patient to ascertain the character and extent of the lung lesions and to follow their development.

Certain densities suggest definite cellular pathology. Etiology is deduced by a study of the entire lung fields, and with a less degree of accuracy a prognosis is made.

The independent X-ray report from a purely laboratory standpoint has great value; but its greatest value is found when it is used to interpret in terms of definite pathology the physical findings by one trained to study the entire economy of the patient. We wish to warn against the reverse method of study, namely, the attempt to study plates in the light of the physical examination and the clinical condition of the patient. Almost any pathology can be read into a plate by a clinician with a keen imagination. Thus the plate reading should be made before the signs and symptoms of the patient are known.

Finally, plates are being read by eminent roentgenologists over our country with very different conclusions. We believe that an effort should be made to correlate our knowledge, and to determine a standard terminology so that at an early date we may arrive at a standard interpretation of X-ray chest plates.

APICAL PLEURITIS AND ITS RELATIONSHIP TO PULMONARY TUBERCULOSIS

A STATISTICAL STUDY OF STEREOSCOPIC ROENTGENOGRAMS OF 366 CONSECUTIVE ADULT CHESTS

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In this report we purpose to study the roentgenological signs which we have learned to interpret as evidences of an apical pleuritis; its incidence, its morphology, and its relationship to pulmonary tuberculosis, and to prove thereby the essentially tuberculous nature of this condition. A study of its relationship to tuberculosis of the tonsil and of the cervical lymph glands has already preceded this in a paper from this laboratory (1).

Our attention was first attracted to this sign by the observation of a rather dense linear shadow lying just beneath the second rib and over the apex of the lung as seen in the stereograms of the chest taken in the routine postero-anterior direction. Observation showed that such shadows are present in a considerable number of cases and that certain suggestive variations of this shadow occur with still greater frequency, shading by insensible gradations from a mere suggestion of a linear shadow to a broad band of reticulation indistinguishable from that of a tuberculous involvement of the subpleural layers of the lung.

The typical shadow is usually found lying just below the lower border of the rib, separated from it by a clear space of from 2 to 4 mm. and perhaps 1 or 2 mm. thick. It is usually continuous for 1 or 2 inches and is commonly lost at either extremity in the shadows of the other structures of the thorax. Under exceptional circumstances it may be traced in those portions of the chest where the conditions are favorable or into the axilla as an extension of the residual shadow of a pleural effusion or empyema. Conditions seem to be unfavorable for its recognition along the border of the soft tissues of the mediastinum or along the anterior and posterior surfaces of the chest wall. Altogether it gives the impression of a tangential view of a thin sheet of connective tissue in the exact position of the pleura over the superior and the lateral-superior surfaces of the apex.

The density of this line is not directly proportional to its thickness but varies through a considerable range. It is generally less dense in the wider examples. The suggestion that the denser and narrower shadows result from the condensation of the broader ones is supported by the evidence of serial plates taken at long intervals, which, in several instances have demonstrated a simultaneous narrowing of the line with an increase in its relative density. The narrowest recognizable lines are obviously of the denser type and may be exceedingly narrow.

The shadows of lesser density are less easily recognized unless they have considerable thickness. In such lines the superior surface is invariably smooth and regular, corresponding with the outline and position of the potential pleural cavity. On their visceral surfaces they frequently are irregular; and careful examination will show tiny projections and elevations extending for 2 or 3 mm. into the lung tissue. This surface is commonly much less dense than the upper, so that some difficulty in determining the exact limits of the shadow arises. Elsewhere small tentlike conical projections may be seen with their bases against the pleura; and from their apices may extend long linear shadows in the direction of the hilum, the whole appearing like "a morning glory with its bell applied to the pleura."

By imperceptible gradations these shadows merge into the well recognized reticular and mottled shadows of an apical tuberculosis, until one cannot determine in how far these opacities lie in the pleura as distinguished from the lung. As a matter of fact, the study of such a series leaves one with the impression that both pleura and lung are involved and that one sees the progressive stages of an invasion of the lung from its pleural surface.

For statistical purposes it was necessary to subdivide this continuous series and to establish certain metes and bounds, however arbitrary they might appear, with the idea of a subsequent redistribution or combination of the various types into fewer and larger classes. Guided by our experience with this shadow we adopted the following classification:

Class A. The "faint line," an exceedingly tenuous linear shadow, seen only in brilliant plates and recognized as definitely within the thorax in a good stereoscopic pair only. The distinctions from the double images produced by thick mirrors and from the double contoured rib shadows produced by imperfect fixation of the chest during the exposure of the plate must be carefully drawn.

This classification was reserved for the instances where there might be difficulty in convincing the unsophisticated eye of the accuracy of the observation.

Class B. The "distinct line," one in which there could be no reasonable doubt, the most conspicuous of the series, of considerable density, and smooth on both surfaces. As already noted, these are assumed to represent cicatrices rather than active pathological processes.

Class C. The "mossy line," one of lesser density, smooth on the parietal surface, but with irregularities of still lesser density appearing to penetrate the interstices of the lung tissues.

Class D. The "proliferating line," one showing tentshaped projections with or without linear extensions towards the hilum of the lung. In most instances, other evidences of tuberculous infiltration are present in the deeper portions of the lung or in the hilum.

Class E. The "obscure line," resulting from the superposition and multiplication of pathological shadows obviously in the lung itself, so that the identification of the pleural element was impossible. These confusing shadows were in all cases those of advanced tuberculosis.

Classes F and G. Those cases in which the field was obscured by intrinsic shadows or by technically imperfect plates respectively.

The observations and classifications were made by three observers familiar with this classification and with the appearances of the "line," working in pairs or in a group of three. The final disposition of any doubtful case was made only on the agreement of all persons. Differences of opinion occurred principally in class A and in the distinction between classes C and D. In the former case conservatism demanded that the case be rejected and thrown into the negative column. As will be noted below, the whole class was finally disposed of in this manner.

As between C and D, the distinction being one of degree largely and therefore arguable, the classification was made only on the agreement of all parties.

Besides the notations on the presence or absence of the "pleural line" in its various forms, observations on the condition of the lungs and the remainder of the pleural cavity were added, that is, the presence of pneumonia, abscess, empyema, pneumothorax, etc. Considerable difficulty arose over a group of 21 cases showing doubtful signs of pulmonary tuberculosis but insufficient to justify that diagnosis. These were classified separately.

All the plates of the chest examinations made during the months of May, June, and July of 1920 were reviewed. They were taken in serial order and without reference to the typewritten records of the clinical or roentgenological diagnosis previously made. The notations were made by serial number only and at no time was the name or clinical record compared with the observations of this study until the final notation had been made.

This three months' period was one that was comparatively free from acute infections and epidemics of respiratory diseases. The material of the roentgenological department comes mainly from the medical outpatient service and the wards of the hospital. In every case the patient had been clinically examined and the suspicion of tuberculosis or other pulmonary disease had justified the examination by the X-ray. Therefore the material is not an accurate cross-section of the population of this district but probably is not very different from the class of patients coming to the ordinary X-ray laboratory.

Where the patient has a record of more than one roentgenological examination, all the records were considered but only the last was included in the tabulation. Such series, however, serve to demonstrate the constancy of the lesion over a relatively long period of time in some cases, while in others there has been a change in the type of the lesion but never a total disappearance. One case presents the sequence of a "negative," a class A, and a class D reading while another demonstrates a recession from a class C to a class B type of shadow. In several instances the change has been one of degree rather than that of type, a distinct line becoming less distinct and vice versa. On the whole, we acquired the impression that class B shadows show less tendency to variation than the others, an assumption in agreement with the idea that they represent cicatrices rather than active progressive lesions.

Practically all the important information derived by this system of classification is contained in the preliminary diagram here reproduced. The original diagram was compiled as follows. A sheet was laid off into rectangles with the right sided lesion arranged to read horizontally and the left sided lesions to read vertically. The significance of the various rectangles is indicated by the marginal letters whose meaning is given in the legend. The case numbers were then introduced into the proper squares describing the condition found. By using the case numbers, it was easy to identify any case which appeared unusual or out of place and to verify the original findings. The cases found in each rectangle were finally enumerated and their totals introduced into a second chart of similar notation, which is the chart here reproduced.

Chart 1

Preliminary Diagram

Right	Left														
	y	*z*	*ay*	*az*	*by*	*bz*	*cy*	*cz*	*dy*	*dz*	*ey*	*ez*	*fy*	*fz*	*g*
w	83	1	9	1	2	2		1		3	1	1			
x	2	2			2							4			
Aw	22		4		2		1								
Ax	6		1	1		2						1		1	
Bw	8				12	2	1	1				1			
Bx	7	2	2	2	3	2	1	1		2		1	1		
Cw	1				2		2			2					
Cx	2				1	1		5							
Dw	1				1		1	1	2						
Dx	4	2	2			2	1	1	1	8		1			1
Ew					1								1		
Ex				1	1	2	2		1	5		20			
Fw						1								6	
Fx						1									
G															13

NOTATION: Letters *a–g*, left sided lesion of class indicated; *A–G* right sided lesion of class indicated; *w*, right lung free from tuberculosis; *x*, right lung with frank tuberculosis; *y*, left lung free from tuberculosis; *z*, left lung with frank tuberculosis.

For statistical purposes the chart needed further condensation and elimination of cases of doubtful or no bearing on the relationships we wished to study. Since the principal interest lay in the connection between pulmonary tuberculosis and the shadows described, all non-tuberculous conditions were excluded. Cases showing evidence of present or past pleural disease not confined to the apex were also excluded on the grounds that the apical shadow might reasonably be supposed to be a part of the general pleural process. It was recognized that some of these were undoubtedly tuberculous in nature, but neither the sequence nor the common etiology could be determined. Similarly the cases showing doubtful signs of tuberculosis were excluded for obvious reasons. Classes E, F, and G were excluded as presenting unsatisfactory data.

Table 1 shows the numbers excluded on these various counts.

Finally, it was found necessary to throw class A into the negative column in the interests of conservatism and classes B, C, and D were combined into one, leaving only two classes with respect to the pleural shadow, namely, a "positive" and a "negative" class, and two classes with respect to pulmonary tuberculosis, namely a "positive" and a "negative" class. This was found necessary because the labor of the calculations involved rapidly increased beyond all reasonable bounds with the multiplication of classes and because the larger groups to some extent reduced the liability of error inherent in the statistical study of limited numbers of cases.

TABLE 1

Selection of cases for tabulation

Total number of cases reviewed		366
Cases rejected:		
For nontuberculous disease	42	
For dubious interpretations	21	
For obscurity of plates:		
Poor technique	14	
Parietal shadows	10	
Confusing pathological shadows	43	130
Cases accepted for tabulation		236

Chart 2

	c-y	c-z	d-y	d-z	
a-w	118 (58.6)	2 (14.6)	5 (25.2)	6 (6.27)	Incidence Expectation
a-x	9 (24.8)	3 (6.0)	2 (10.2)	2 (2.6)	Incidence Expectation
b-w	10 (35.5)	0 (8.8)	21 (15.3)	6 (3.8)	Incidence Expectation
b-x	17 (13.7)	6 (3.4)	7 (5.9)	22 (1.5)	Incidence Expectation

NOTATION: *a*, right pleura free; *b*, right apical pleuritis; *c*, left pleura free; *d*, left apical pleuritis; *w*, right lung free from tuberculosis; *x*, right lung with frank tuberculosis; *y*, left lung free from tuberculosis; *z*, left lung with frank tuberculosis.

Chart 2 is the result of such condensation. It gives all the combination possible in a person having two pleura and two lungs, any one of which may or may not be diseased, and in this chart are tabulated all the cases that meet the requirements previously laid down.

This chart (like the others) is symmetrical with respect to the diagonal running from the right upper to the left lower corner and the rectangles intersected by this diagonal represent the cases with symmetrical lesions. The rectangles to the left and downwards of this line represent cases with predominantly right sided involvement while those on the right and above the line represent predominantly left sided involvement.

Cursory examination of this chart shows a number of interesting observations. For instance, exactly one-half of the cases listed after the exclusions just noted, were free from any evidence of pathology in the lungs or pleurae. When one includes the 43 cases of advanced tuberculosis excluded because of the confusion of shadows (see table 1), the 21 excluded because of the doubtful significance of observed shadows in the lungs, and the 42 cases of pleural and "nontuberculous disease" omitted, one finds that only 34 per cent of the total number of plates with satisfactory radiographic records escape all suspicion of trouble in the chest.

In distribution the lesions are obviously more numerous on the right side, and the totals in the rectangles on the diagonal line (symmetrical lesions) are conspicuously large with the single exception of the rectangle *a-x-c-z*. The highest totals occur at either extremity of this diagonal.

The significance of these features and the relationships they imply are not clear to casual inspection or simple tabulation because we have no criteria with which to compare the incidences in each group. Causal relationships or the consequences of common causes can be demonstrated only if it can be demonstrated that the distribution of the lesions is other than that which one would expect to find if a similar number of lesions were to be distributed among a similar number of individuals by the simple laws of chance. Fortunately, such a comparison is possible since the calculation of such a distribution is reached without great difficulty.

For the sake of the demonstration of the principle involved we may take the relatively simple questions of the frequencies of occurrence and the relationships of the apical pleuritis on the right alone, on the left alone, and bilaterally (see chart 3).

From chart 2 one may compile the cases of the *a-c* group falling in the four rectangles *a-w-c-y*, *a-w-c-z*, *a-x-c-y*, and *a-x-c-z*, that is, 132 cases representing the number of individuals with a pleural shadow in either apex. Similarly the *a-d* group contains 15, representing the individuals having a unilateral left pleuritis. The *b-c* group numbers 33 with a unilateral right pleuritis and the *b-d* group with a bilateral pleuritis numbers 56. This is a total of 236 cases for the entire series.

Each of these individuals has a right and a left pleural cavity. Out of the 136 right pleurae, 33 are involved alone and 56 are involved with the left or a total of 89 times out of a possible 236. The incidence of right pleural shadows is therefore 89 ÷ 236 = 0.3771 (see table 2). This may be termed the "rate of expectation" for the individuals of the whole group to this specific lesion. The "rate of expectation" of his escaping this lesion is 1.000 − 0.3771 = 0.6229. These rates may be designated "b" and "a" respectively in harmony with the indices of the chart.

Chart 3

Tabulation of the four possible combinations of pleuritis giving actual incidences and expectations on the theory of chances. Notation as in Chart 2

	c	*d*	
a	132 (102.8)	15 (44.2)	
b	33 (62.2)	56 (26.8)	
		Total	236

TABLE 2

Incidences of pleuritis and pulmonary tuberculosis

	NUMBER OF CASES	RATE	LETTER
Right apical pleura normal	147	0.6229	*a*
Right apical pleuritis	89	0.3771	*b*
Left apical pleura normal	165	0.6991	*c*
Left apical pleuritis	71	0.3009	*d*
Right lung normal	168	0.7119	*w*
Right pulmonary tuberculosis	68	0.2881	*x*
Left lung normal	189	0.8008	*y*
Left pulmonary tuberculosis	47	0.1992	*z*

The values of "c" and "d" are calculated in a similar manner and found to be 0.6991 and 0.3009.

The total expectation for the individual right pleural cavity is expressed by the equation

$$a + b = 1 = 0.6229 + 0.3771.$$

The expectation for the left pleura is expressed by the equation

$$c + d = 1 = 0.6991 + 0.3009.$$

The combined probabilities for the individual having two pleurae and taking two chances is expressed by the product of the two equations, that is,

$$(a + b = 1)\,(c + d = 1) = ac + ad + bc + bd = 1.$$

The value of ac represents the expectation of any individual of escaping all involvement, ad the expectation of having the right free but the left involved, bc of having the right only involved and bd of having a bilateral involvement of both pleurae.

The expectation for the entire group is obviously equal to the rate of expectation for the individual multiplied by the number of individuals in that group. Thus the number of cases one would expect to find having a bilateral involvement out of a group of 236 would be represented by the expression.

$$236 \times \mathrm{b} \times \mathrm{d} = 236 \times 0.3771 \times 0.3009 = 26.8.$$

Similar values for the three remaining groups have been calculated and introduced in parentheses in chart 3.

Reference to this chart shows that if the lesions had been distributed without relation to each other and purely as by chance, one would have expected to find 102.8 cases without pleuritis in either apex, which is 29.2 short of the actual incidence. Similarly one would have expected to find 26.8 cases with bilateral involvement, which is again 29.2 short of the actual. On the other hand, the unilateral lesions are less numerous than the expectation by exactly the same total number.

Obviously this distribution is not by chance, but the existence of one lesion influences the development of the second, either by predisposing to involvement of the opposite side or by protecting against such extension. The direction of this influence may be inferred from the direction of the resulting dislocation of the groups in the series.

If one conceives of the total number of lesions being distributed to a group of 236 cases, the assignment of an unusual number of lesions to individuals already having one lesion will at the same time produce an excess of those having two lesions and will rob an equal number of individuals of the one lesion to which they are entitled on the doctrine of chance. The result is a dislocation of an equal number of cases toward the ends of the scale and away from the middle, that is, an excess of those that escape and of those with bilateral lesions and a deficit in the groups with the unilateral involvement. If, on the other hand, one lesion protects the individual against the development of a second, certain of the lesions which would have gone to individuals already having one will be assigned to individuals that have a right to expect to escape, with a resulting dislocation of numbers from the ends and towards the middle.

In the series under consideration, the former conditions obtain, and we cannot escape the conviction that the occurrence of one lesion predisposes toward the second.

In chart 2 the values of the group expectations calculated on the foregoing principle, but for four conditions, have been introduced in parentheses in the corresponding rectangles, and the data necessary for the calculations are included in table 2.

This chart, while at first glance rather intricate, is really very simple. For example, the number 21 in the third rank and the third file of the chart represents the actual number of cases having found the specifications *b-w-d-y*, which reference to the legend proclaims have a pleuritis on the right side, no pulmonary tuberculosis on the right side, a pleuritis on the left and no tuberculosis on the left; in other words a bilateral apical thickening without evidence of pulmonary tuberculosis. The number 15.8 in parentheses in the same rectangle is the number one would have expected to find in this group on the hypothesis of a distribution of the lesions on the doctrine of chance.

An examination of chart 2 shows a similar dislocation of numbers as was noted in chart 3, namely, an excees in the left upper rectangle representing the negative cases, a minimum as compared with the expectation in the rectangles adjoining, and a gradual but not uniform increase to the maximum ratio in the right lower rectangle consisting of cases with involvement of both lungs and both pleurae. This is exactly the type of dislocation that would be expected to result if the presence of one lesion predisposes to further involvement.

For the further study of the relationships between the various groups represented in the chart it would be well if we could find a numerical expression for the tendency or "predisposition" on the part of the individual towards the various combinations. Such a measure is not at hand. The ratio of the incidence to the expectation is not such a measure, since it depends not alone on the tendency of one group to the acquisition of an additional lesion but on the balance between the tendencies to gain numbers on the one hand and to lose on the other.

It is quite impossible to study all of the possible consecutive steps in the scale from no lesion to 4 lesions because these number no less than 32, and we have no way of distingiushing the sequence by which any case has arrived at its present stage of development. If one groups the combinations of lesions as groups of the zero, first, second, third, and fourth orders according to the number of lesions present, we find four possibilities between the zero and the first orders, 12 between the first and second orders, 12 between the second and third orders, and 4 between the third and fourth orders.

Chart 4.

Ratios of incidence ÷ expectation in the groups of Chart 2. Notation as in Chart 2

	c-y	c-z	d-y	d-z
a-w	2.0	0.14	0.197	0.96
a-x	0.87	0.47	0.20	0.77
b-w	0.27	0.00	1.38	1.37
b-x	1.24	1.77	1.18	14.60

TABLE 3

Association of lesions arranged by "orders"

	INCIDENCE	EXPECTATION	RATIO
No lesion (zero order)	118	59.0	2.0
One lesion (first order):			
Unilateral pleurisy	15	61.0	0.25
Unilateral pulmonary tuberculosis	11	40.0	0.28
Two associated lesions (second order):			
Bilateral pleurisy	21	15.0	1.4
Homolateral pleuropulmonary	23	20.0	1.1
Bilateral pulmonary	3	6.0	0.5
Contralateral pleuropulmonary	2	19.0	0.1
Three associated lesions (third order):			
Bilateral pleural plus unilateral pulmonary	13	9.0	1.4
Unilateral pleural plus bilateral pulmonary	8	6.0	1.8
Four associated lesions (fourth order):			
Bilateral pleural plus bilateral pulmonary	22	1.5	14.6

One can, however, study the deviations from the uniform gradient in the ratios of the groups within the different orders, and so point out those conditions which have a tendency toward stability or otherwise, as compared with the other members of the same order. These ratios have been calculated and charted in chart 4. In table 3 are given in tabular form the calculations of these ratios for certain relationships within groups of the same order.

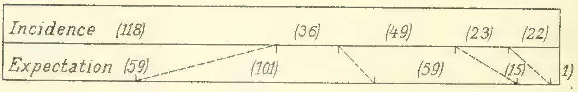
Our use of the term "rate" in the foregoing paragraphs will probably offend the meticulous mathematician, since a "rate" ordinarily involves a time element. As a matter of fact the time element is present in our problem and the rate which we have calculated represents the average rate for a time interval equal to the average age of our patients. Data are not available to do otherwise. What we have done is to calculate a specific average rate against a constant but unknown time element. The relation of the two is shown in the familiar law of elementary physics:

$$\text{velocity} \times \text{time} = \text{space}.$$

In such an equation we have assumed that the time element remained constant and the velocity varied as the space. One might with equal justice assume that the velocity remained the same and the time element varied with the space with identical numerical results.

Chart 5

Illustrating the relative time interval occupied by each stage of invasion on the assumption of a uniform rate for all individuals in the group.



With this conception of our problem the actual number of cases occurring in the groups of different orders may be taken as an expression of the relative average time interval occupied in that particular stage of the disease in its progress up to the average age of the group (see chart 5). We may therefore say that the average time interval elapsing before developing the first lesion is "118 units," the value of the unit being undetermined. This average includes individuals that will never be affected as well as those who have already progressed to the more advanced stages of the disease. The average time interval for the second stage, having one lesion, is represented by 36 units, etc. The theoretic intervals on the basis of the doctrine of chance are given in the chart by the subdivisions of the line below.

Comparing the two sets of values we reach the conclusion that the average individual remains free from the disease twice as long as one would expect. Once he becomes involved by the first lesion he quickly develops the second, remains for a longer period in this stage, and after acquiring his third, still more quickly completes the catalogue,—all of which is quite at variance with the schedule calculated on the basis of chance.

It should be noted that a truer conception of the duration of the final stage would be reached if one were allowed to include the 42 cases of advanced pulmonary tuberculosis which were rejected because the apical pleurae could not be satisfactorily observed in the confusion of pathological shadows in the upper lobes (see table 1).

The conclusion is the same, namely, that there is a definite relationship between all these conditions, that the progress of the disease is not regular but that there is a relative stability in the two lesion stage, as shown by the relative numbers of cases falling in each class.

Some light is thrown on the question of the probable sequence of these lesions by the frequencies of the pleural and pulmonary lesions. In table 3 one sees that the pleural lesion occurred unilaterally in 15 cases and bilaterally in 21 cases, with a total of 42 lesions in the latter class or a grand total of 57 pleural lesions uncomplicated by pulmonary involvement. Only 11 cases presented a unilateral pulmonary tuberculosis and 3 a bilateral disease uncomplicated by pleural lesions; a total of only 17 tuberculous lungs. The conditions of the problem are altogether against the discovery of the pleural lesion, since the line can be seen clearly only over a limited area of the apex. Could one adequately explore the entire surface of the upper lobe, the incidence of the pleuritis might be expected to be still greater. Moreover, reference to the original protocol (preliminary chart) demonstrate that of the 17 uncomplicated tuberculous lungs no less than 10 were originally given a class A pleural line and were subsequently thrown into the negative column in the interests of conservatism.

The greater liability to involvement of the pleurae is more convincingly shown by table 2, there being a total of 89 right apical pleuritis as against 68 right pulmonary tuberculosis; and 71 left apical pleuritis as against 47 of left pulmonary tuberculosis.

From the apical pleura of the one side to the apical pleura of the other side appears to be an easier step than to the lung of the same side, if one may judge by the ratios of table 3, although the difference is not very great. The ratio is considerably greater for involvement of the right lung with a pleuritis of the same side than for a similar combination on the left side. By contrast the step from the apical pleura of one side to the lung of the other seems to be relatively difficult, since the ratio for the involvement of the right lung with the left pleura is nil and of the left lung with the right pleura is only 0.1, the next lowest value.

It would seem therefore, that, in the typical case, the progress is from the pleura of the one side to the pleura of the other side, and to the lung of the same side, but that the involvement of the lung of the other side depends on the preliminary involvement of the overlying pleura. The only conceivable alternative is that of an overwhelming instability of the contralateral condition leading to a very prompt promotion to a group of the next higher order. Such a conception lacks probability.

Finally, the high rate of the "four lesion" stage may be interpreted as an expression of its terminal character, and, as already noted, this high ratio probably does not correctly indicate the size of this group because of the exclusions.

We believe that the evidence here presented justifies the conclusion that there is a definite etiological and chronological connection between the apical pleuritis here described and pulmonary tuberculosis. We wish to draw a sharp distinction between this "apical pleuritis" and the linear shadow which is seen as a continuation upwards of the pleural density that so regularly follows empyema. We do not, however, exempt the pleural line that is also quite regularly seen over the opposite apex in cases of pleural effusions and hold it probable that it represents a tuberculous lesion. Its significance seems to be worthy of further study.

The acceptance of this view does not simplify the problem of the diagnosis of clinical tuberculosis. Its frequency in apparently healthy individuals makes it probable that it often represents a healed lesion, and it would be manifestly unjust to condemn every bearer of a "pleural cap" to the social and economic restriction of the tuberculous life. On the other hand, the occasional occurrence of cases of hemoptysis with no other sign, either physical or radiographic, goes to prove that it is not entirely without significance.

The relative stability of the condition when both apices show the line without involvement of the underlying lung, especially when the density of the shadow suggests a cicatrix, makes it probable that the pleurae present a considerable barrier to the progress of the tubercle bacillus. The clinical evidence in these cases suggests that the class B line is relatively harmless if found alone. Classes C and D, however, leave us with the impression that the process is not entirely confined to the surfaces of the pleurae and is not completely cicatrized and they are regarded as distinctly suspicious of serious trouble. In any event, the occurrence of the line may be accepted as an evidence of a preceding lodgment of the bacillus and an inflammatory reaction at that point.

In looking for an explanation of the early involvement of the apical pleurae and the infection of the lungs by the transpleural route, we have found no explanation so satisfactory as that suggested in the previous paper from this laboratory, namely, the infection of the pleurae through the lymphatics of the neck presumably through the lymphadenoid tissues of Waldeyer's ring. The asymmetry of the lymphatic anatomy serves to explain adequately the preponderance of right sided lesions; the closeness of the relationships of the cervical lymphatics to the apical pleurae explain the usual apical distribution of tuberculosis as no other theory will; and the phenomenon of pleurisy with effusion requires only the concept of an apical lesion with a serous exudate which gravitates to the lower thorax and spreads the infection, to find a satisfactory explanation.

We do not mean to imply that this is the only route of infection of the lungs by the tubercle bacillus. In fact there are exceptions to the apparent sequence in adults and the prevailing distribution of the condition in children seems to point to some other mechanism. In fact, it is not impossible that the lymphatic drainage in the adult departs in important particulars from that prevailing in childhood. Certainly roentgenologists will agree that the adult picture of chronic pulmonary tuberculosis is extremely infrequent under puberty. It is not impossible that the differences in distribution depend on differences in the route of the infection rather than on differences in the reaction of the individuals at the different ages.

CONCLUSIONS

1. Pleural shadows over the apices in various forms occur with great frequency.
2. By insensible gradations these shadows pass into those of frank pulmonary tuberculosis.

3. The demonstrated association with pulmonary tuberculosis demonstrates a prevailingly tuberculous nature.

4. Chronologically the apical pleuritis precedes the pulmonary involvement.

5. The prevailing tendency to spread is (a) to the opposite apex and (b) to the underlying lung.

6 The infection probably reaches the pleurae through the cervical lymphatics.

We wish to express our obligations and appreciation to Drs. C. V. Weller of the Pathological Department, and L. H. Newburgh of the Department of Internal Medicine, as well as to Drs. J. A. Herring and E. F. Merrill of the Department of Roentgenology.

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TUBERCULOUS EMPYEMA[1]

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Tuberculous empyema, while recognized as a serious complication, is very inadequately dealt with in works of reference.

In discussing the subject with those interested in tuberculosis a wide difference of opinion is found as to treatment and results; and very few appear to know of the advantages of the treatment to be referred to later on.

Keen in volume 3 of his *System of Surgery* says, The "advisability of operation on tuberculous empyema is open to question. It is advisable to delay operation until spontaneous rupture is imminent."

Burghardt's *System of Operative Surgery*, volume 3, page 721, says, "The presence of tuberculous disease generally, though not invariably, prevents the closure of an empyema, even if the size and shape of the cavity as such are favorable for a cure." It goes on to say that, if the patient's general condition be good, advise thoracoplasty, at the same time warning the patient that the operation will probably be unsuccessful.

Kessel and Tishman report seven cases of effusion, five of which contained tubercle bacilli, treated by aspiration with unfavorable results.

Shortle remarks that "from Muralt to Saugman and Brauer, observers are agreed that antiseptic injections into exudates are no good." He reports one pus case with tubercle bacilli, with the patient drained three times and now symptom free, but the complication still persisting. He advocates watchful waiting and drainage, probably by aspiration.

Bullock and Twichell, quoting Muralt, say, "The exudate may look ugly and grayish and contain tubercle bacilli without calling for surgery." They speak of the seroimmunizing effect of the serum, that is, the exudate contains antibodies and therefore may be valuable to the patient. They further say, "True empyemas with marked clinical symptoms need plastic operations. If small, twenty to thirty cc. of electrargol sometimes arrests the process."

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[1] Read before the Trudeau Society of the Los Angeles County Medical Society, February 21, 1921.

Matson uses a one to five thousand potassium permanganate solution as an irrigation with success.

It is interesting to note Peters's report of cases of artificial pneumothorax, showing sixty-five per cent with effusions. He says that if continued long enough there will be one hundred per cent with effusions, and, in a series of seven hundred cases in foreign literature, he reports a percentage of 7.71 with pus showing the tubercle bacilli alone.

Capps's excellent article in the *Oxford System of Medicine* says, "Tuberculous empyema has a bad outlook. Draining by the aspirating needle may mitigate but does not cure. Thoracotomy is indicated only when the exudate is small and the strength of the patient is reasonably good. The operation is likely to light up the tuberculous lung, and hasten the end. In the presence of pulmonary lesions the clinical indication should be to give symptomatic relief, and this is often accomplished by aspiration."

Tuberculous empyema is definied by Duboff as a purulent effusion into the pleural cavity, in which the bacillus of Koch is the sole or predominating microörganism. Duboff's article in the AMERICAN REVIEW OF TUBERCULOSIS, volume 3, page 590, is extremely good, although his experience is quite different from my own. For instance, he says that every case of tuberculous empyema, occurring in a patient receiving the pneumothorax treatment, is due to a distinct spontaneous pneumothorax occurring in the lung under collapse. This has not been the case in my experience so far. I have seen but one definite spontaneous pneumothorax in the collapsed lung, and this was not followed by empyema. Duboff says that conservative treatment is the best, together with noninterference, as long as possible, with aspiration to relieve pressure symptoms and prevent sinus formation. He says the prognosis is bad. Of his 20 cases of empyema, 4 ruptured into a bronchus, and 6 burst through the chest wall.

Peron, quoted by MacCallum in Osler's *Modern Medicine*, distinguishes two types of pleural tuberculosis: first, pleuritis tuberculosa serofibrinosa, and, second, empyema tuberculosa. In my experience in the first class tubercle bacilli are seldom found in the effusion and in the latter they are always found. There is, however, a third type, the miliary.

Tuberculous empyema may occur (1) in pneumothorax either spontaneous or artificial, (2) from a ruptured tuberculous abscess of the lung without pneumothorax, and (3) from a rupture of a peribronchial lymph node. The character of the early exudate is a clear serous fluid with no microörganisms. Cultures and guinea pig inoculations may both also be negative. Later the fluid becomes opaque and turbid, with polymorphonuclear leucocytes predominating, and the tubercle bacilli nearly always to be found. Communication with the bronchus may or may not cause a mixed infection.

The onset is usually definite with severe pain in the side and a sharp rise of temperature which may subside as the effusion develops. A gradual onset occasionally occurs with no definite history at the beginning. The temperature may or may not be elevated, even when large quantities of pus are present, which is often remarkably well tolerated for long periods without any symptoms of toxaemia.

West, quoted by Brown in Osler's *Modern Medicine*, advocates free incision as soon as the diagnosis is made, while Lord, in the same work, says that radical operations are not to be considered, but that resort must be had to palliative measures of aspiration or siphon drainage.

Baümler advocates thoracotomy when pus-forming germs are present; but when the tubercle bacillus alone is present or the exudate is sterile and pressure symptoms are present, aspiration followed by thoracotomy when the general condition improves should be performed.

Of 35 cases of tuberculous empyema operated on by Küster 9 recovered, 6 were not cured and 16 died. In Schede's collection of 45 cases, 10 were cured and 35 died. Lord had 12 cases with sterile exudate; 1 showed tubercle bacilli, 3 died in the hospital, and all but 1 have since died, and this one has a discharging sinus, but is otherwise apparently well. Murphy says that once you have opened the abscess cavity in these late cases it will never close spontaneously.

In the past four years we have had under our care 12 cases of this dreaded complication. One of these was terminal, one moved away during treatment and his subsequent history is unknown, and a third was a far advanced case of organic heart disease and soon died, leaving 10 cases to be considered. Two of these were treated by thoracotomy and both died with their complication unbenefited. In fact the end was hastened by the very means taken to cure them. Of the 7 remaining all are alive, and all have been relieved of their complication. Two of these were what may be called spontaneous empyema, and 5 occurred during the course of treatment by artificial pneumothorax. They were all treated by the method instituted by Murphy many years ago, which has fallen into undeserved neglect. This plan was first brought to my attention by Dr. Willis R. Smith of El Paso, Texas.

Method. All of the purulent material that is possible is removed by aspiration or siphonage or both combined, using a large needle. Then, from 1 to 12 ounces of a 2 per cent solution of formaldehyde in glycerine is injected, the amount varying according to the amount of fluid withdrawn. One never introduces more than half the volume withdrawn, and is careful the first time to inject too little rather than too much. Air is then introduced until the manometer reading is near the negative point, or, if it is a case of artificial pneumothorax, the pressure is raised to that usually given this particular patient. In from forty-eight hours to one week after the first treatment, the patient is again aspirated, usually of about twice as much fluid as was injected, the character of which will be altered by having become seropurulent. More of the formaldehyde-glycerine is again injected, and in from three to ten days again removed. This is continued until the character of the exudate changes to serosanguinous, when it is sterile and should be left, as it is harmless and will ultimately be absorbed. This treatment varies a little from that of Murphy, who advocates the introduction of only one half-ounce of the glycerine-formaldehyde solution.

Each treatment is followed by a more or less violent reaction. The temperature rises as high as 103°, with pain and discomfort in the region affected. It, however, rapidly subsides, and in two or three days the patient is as comfortable as before the treatment.

Billings reports a death following this injection, but we have seen nothing particularly alarming in those we have so treated.

Murphy, in his *Clinics* of 1915, says of the formaldehyde-glycerine solution:

> First, it kills the microörganisms in the pus, secondly, it keeps up the polymorphonuclear leucocytosis. These indicate the increase in the number of phagocytes and the formation of serum that contain trypsin which is similar to the pancreatic trypsin and converts albuminoids into albumoses,which are soluble, and the absorption of the exudate is begun.

In the *Journal of the American Medical Association* for July 27, 1920, Rinehart and Oelgoetz report the treatment at Camp Sherman of ordinary empyema with the formaldehyde-glycerine solution with perfect results. The amount of the solution used is not mentioned.

In the same journal of December 1, 1918, A. E. Mozingo reports the use of this solution in nontuberculous empyema to finally sterilize the pleural cavity after first treating it with Dakin's solution. His methods are certainly thorough, to say the least. He irrigates the pus cavity every two hours during the day, and every three hours at night with the Dakin's solution for the first one to four days, and then at longer intervals. He says that with the formaldehyde-glycerine solution the cavity becomes sterile in from one to seven days. The reason for using the Dakin's solution at all is obscure to me, as it fails to sterilize. One would ask why the treatment is not begun with the formaldehyde-glycerine solution.

SUMMARY

First, authorities are generally unanimous that tuberculous empyema is dangerous to life and hopeless as to recovery. Second, those who have tried the Murphy treatment report excellent results, so that it should be given a fair trial in the endeavor to alter this hopeless outlook.

The following is a brief résumé of two of our cases receiving the above treatment. The first is a case of spontaneous empyema occurring in a chronic tuberculous patient.

M. M., aged twenty-two, bookkeeper, consulted me with active tuberculosis of both apices in September, 1916. He came to California in November of the same year, where he entered a nursing home, remaining there under treatment for six months and returning east the following summer. He has since spent his winters in California and has worked at various occupations most of the time, although with more or less activity in his lungs. In November, 1919, while employed as a bookkeeper in a bank, he was taken with an acute attack of pleurisy with effusion in the left side, which was at the time the active side. He gradually recovered and returned to work, although still carrying his effusion. As he was short of breath, aspiration and replacement of the fluid with air were advised to relieve his pressure symptoms and to determine the character of the exudate. In March he finally consented and 5 pints of pus rich in tubercle bacilli were removed, and 12 ounces of the formaldehyde-glycerine solution and 700 cc. of air introduced. One week later 23 ounces of seropurulent fluid were removed and 8 ounces of glycerine-formaldehyde solution and 300 cc. of air introduced. Twelve days later 17 ounces of cloudy serosanguinous fluid were taken out and 4 ounces of glycerine-formaldehyde solution and 200 cc. of air introduced. One week later a small amount of serosanguinous fluid was removed and no more antiseptic put back. He has since gone back east, and has had no return of his empyema.

The second case is one developing during treatment by artificial pneumothorax:

Mrs. R., age twenty-four. Has been in poor health about two years. Has been treated for liver trouble, has lost about 20 pounds, now weighs 90 pounds, temperature at times reaches 103°. Right lung shows evidence of a healed lesion in apex. Left lung has an active tuberculosis throughout with a large cavity above the second rib. As she showed very little improvement after several months' treatment it was decided to attempt a collapse without much hope of success as the pleura, as shown by the X-ray, was greatly thickened, and probably adherent. Contrary to our fears the pneumothorax was successful, the temperature fell to normal, her weight increased, the cough and sputum almost disappeared, and the latter was negative for tubercle bacilli most of the time, so that everything looked favorable for an arrest of her trouble. After eight months' treatment she was taken with severe pain in the affected side with fever. Empyema was found and 36 ounces of pus were removed and the glycerine-formaldehyde solution introduced. This treatment was continued until the fluid became serosanguinous. Soon afterwards she became pregnant, and after an uneventful pregnancy was delivered normally of a healthy child, her first, and has remained free from the empyema since.

THE CAMPAIGN AGAINST TUBERCULOSIS[1]

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While the final object of any antituberculosis program is the complete elimination of tuberculosis, it should be recollected at the outset that this is not to be accomplished by seeking to obtain complete disappearance of the tubercle bacillus, a truly ubiquitous organism, but rather by arriving at conditions which will render this germ innocuous.

Frederick L. Hoffman in a recent article which appeared in the *Spectator* refers to the greater prevalence of tuberculosis in general during the past few years. He says:

> The increase since that year (1913) to the end of 1918 is, of course, primarily attributable to the far-reaching consequences of the Great War. But the wholly unexpected and material reduction in the rate during 1919, or from 153.2 in 1918 to only 121.7 in 1919, cannot be considered otherwise than as measuring in part the direct effect of concerted and more strenuous methods of treatment and control.

Mr. Hoffman further shows that the decline of the tuberculosis death rate in the principal American cities has been in striking contrast with a positive increase in England and Italy during the last five years.

The favorable effect of the campaign against tuberculosis in the United States during this period has been clearly attributable to the combined efforts of official health bodies—national, state and municipal—and non-official civic societies, including the national, state, and local tuberculosis societies. As these united forces grow in strength and efficiency, better results than have been achieved in the past may be confidently expected in the future.

Much will depend upon the degree of perfection of the various state tuberculosis societies, as working machines or organizations, so far as their accomplishments hereafter are concerned. In each state the aim should be to create units on a county wide basis, except in the case of the smaller and more sparsely populated counties, which might be grouped into units embracing two or possibly three counties. Each unit should endeavor to provide all of the machinery necessary for the control of tuberculosis so far as education and prevention are concerned, thus aiding materially the state health departments in the work of diagnosis and treatment.

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[1] Abstract of the Presidential Address before the Annual Conference on Pennsylvania Tuberculosis Problems, Philadelphia, January 16 and 17, 1921.

I have a fixed belief that the rural communities are just as much in need of an educational program with regard to the subjects of tuberculosis and better hygienic living as are our towns and cities. It is hoped, therefore, that those engaged in the warfare against tuberculosis will appreciate the importance to success of effective county wide organizations as units. I would further urge the representatives of local organizations to conduct their tuberculosis work on a true business basis, so that they may account to the public for funds raised in the annual seal sales. Everywhere there is also need of a closer, more effective coördination of public and private resources.

The prophylaxis of tuberculosis so far as the work of state civic societies extends, involves two main elements, (1) the building of a maximum individual resistance and (2) education of the public with regard to the nature and modes of preventing the spread of the tubercle bacillus. Educational appeals are applicable to both of these divisions of the subject, but the character of the instruction to be offered differs with respect to certain more or less important details.

1. The building of a maximum resistance. It must ever be kept in mind that the maintenance of a high standard of physical vigor is the most efficient method of preventing tuberculosis. This is to be brought about largely by the education of the public, more especially the children of our public and parochial schools in matters of health. In connection with the modern Health Crusade that is being carried on, many tuberculosis societies are doing a splendid and well-conceived educational work in this direction.

It is becoming clear to educators that personal hygiene must be included in any system of public education at the present day. Fortunately too, some American colleges and universities have recently introduced courses of instruction in this subject. While it is gratifying to note this innovation, personal hygiene should be universally taught not only in our public schools, but also in our institutions of higher education.

In the prevention of tuberculosis, however, we must also search for and overcome or ameliorate the many predisposing factors that too often lie in the environment. I refer to physical defects, overwork and overstrain which lead to breakdown with tuberculosis, badly built, ill-ventilated school houses, poor housing conditions at home, public and individual uncleanliness, lack of proper food and the like.

In our general campaign of education these various predisposing factors must receive attention in connection with the information given out to the public along the lines of personal hygiene and sanitation. In passing, the fact should be emphasized that the matter of improving housing conditions is a most insistent and important part of the social prophylaxis of tuberculosis. Moreover, it is a problem that affords local tuberculosis organizations an excellent opportunity for real service to the community through the creation of a proper public sentiment with regard to the existing housing shortage and other aspects of the question.

As practical antituberculosis workers, we must likewise accept and keep in mind the view of childhood infection, which confers a considerable degree of immunity against external superinfection in adult life, as well as the extreme latency of the disease. While we often fail to head off infection in childhood, it is possible (and this should be our aim) to build up resistance and thus prevent latent tuberculosis from developing into active disease later in life. By rendering the soil unsuitable for the growth and development of the tubercle bacillus we accomplish prophylaxis. The correct conception of the foregoing facts has an important bearing upon our attitude toward the problem of prevention of tuberculosis.

Without doubt, we have been expending too much misdirected effort upon the question of the prevention of adult infection, in view of the widely accepted belief that in the majority of the cases this probably occurs early in life. This fact, however, does not preclude an efficacious plan of prevention, since by building up bodily resistance we render the germ harmless.

In the control of tuberculosis, which is a community problem, the coöperation of physicians should be sought. It is true that many problems challenge the attention of the physician at the present day, but to his credit be it said that he is ever willing and often eager to bear his share of the burden in this communistic age. By experience and training he is or should be well fitted to assume an important rôle in any social campaign against tuberculosis, and his services should be secured by local committees and county organizations throughout the states to the fullest extent. I realize the fact that physicians are doing a fair share of work in many localities: my plea is for a more general participation on the part of physicians and, let me add, health officials who are also well qualified to help solve the tuberculosis problem. From the standpoint of success, much depends, as before stated, upon the completeness of an antituberculosis program; and both physicians and sanitarians can be relied upon as a rule to give valuable aid in its formulation and projection. In many cases they may be called upon as specialists to carry out certain parts of the program, for example, to give public addresses on various phases of the subject of tuberculosis prevention and also technical advice with regard to hygienic and sanitary questions as they arise.

Here attention should be called to the nutrition clinic for the undernourished, of the great utility of which as a means of building up resistance there can be no question. Unfortunately, it is obviously impossible for financial and psychologic reasons that all in need of its advantages can be served, but wherever found to be feasible, it should be instituted. We should not, therefore, base our antituberculosis campaign on the nutrition clinic alone.

It is axiomatic that whatever improves the health of a community operates to lessen the prevalence of tuberculosis by increasing bodily resistance. The diffusion of popular knowledge in matters of health should therefore be actively carried on by all civic and professional bodies, including tuberculosis societies. There are two agencies which I have long felt have not been utilized to the degree which they merit. These are, newspaper publicity and the placing in private homes of literature in a form suitable for preservation. Obviously, since urban populations are as a rule polyglot the literary matter would, sometimes at least, of necessity have to be printed in different languages.

While it is not the purpose of this paper to attempt an evaluation of the daily press as an educative factor, I hold that it is potent as a means of popularizing scientific knowledge when the latter is taken from authentic sources. Matter carefully prepared in concise form should be published in the daily and weekly newspapers and, as far as possible, without change, thus obviating the giving out of misinformation which is so hurtful in its effects. Expert opinion is coming more and more to realize the practical importance, for reasons of public health, of carefully guarded newspaper publicity, so that I would urge upon workers throughout the country to make available in this manner to the public constantly reliable knowledge on the subject of tuberculosis.

In this connection so called health caravans as an aid to educational efforts are worthy of mention. The necessary details of this method of carrying on tuberculosis and public health work are to be found in a recent volume by Mary Swain Routzahn entitled *Travelling Publicity Campaigns*, published by the Russell Sage Foundation. The information and suggestions contained in this book should merit the attention of the Pennsylvania Tuberculosis Society.

2. Education of the public with regard to the nature and prevention of the spread of the tubercle bacillus. General prophylactic measures from the standpoint of the prevention of the spread of the tubercle bacillus must be directed primarily against the bovine bacillus which has been found in 6 per cent of samples of milk collected for bacteriological examination (Humbert). Suspected herds demand veterinary inspection and the slaughter of any diseased animals that may be found. In view of the recent observations of Brownlee who noted remarkable correlations between bovine tuberculosis and tuberculous peritonitis and meningitis in children, this subject should engage the earnest attention of rural tuberculosis committees and branch societies everywhere.

The employment of the visiting nurse, who is as a rule well qualified to do tuberculosis work, by each unit or county branch society is to be strongly advised and encouraged. Both as regards the giving of prophylactic advice, which should constitute her main labor, and the demonstration of the proper application of relief measures, the visiting nurse should be required to render a daily report, at short intervals, to the local committee or county branch. To be most effective she should also be in affiliation with an organized dispensary or state clinic for which she should make the social investigations and examinations which are so helpful to the physician in charge and enable him to complete his casecards. This plan would also possess the advantage of locating cases of tuberculosis and at the same time afford access to the patient's family, which must always be dealt with suitably, if we would prevent dissemination of the tubercle bacilli.

It is in this connection that the visiting nurse can give useful advice with regard to the disposal of the sputum. More important still, she may be able to have all other members of the household in which a case of tuberculosis exists examined in order that physical defects and conditions of subnutrition may be detected and then remedied. It will be recollected that (as stated above) those members of the patient's family who are apparently healthy may be subjects of a latent infection which occurred in childhood. Hence, to prevent a flare up of the disease in the latter, the bodily resistance is to be maintained constantly at the maximum level.

One of the chief methods of preventing the spread of tuberculosis is by isolating cases, that have reached the infective stage, in sanatoria, special hospitals, or sections of general hospitals. Isolation for the entire course of the infective stage, however, is impracticable. On the other hand, advanced cases of pulmonary tuberculosis among the dependents, which are a distinct menace, demand institutional care. In certain states, for instance, New York and Massachusetts, this needy and important class is accommodated in special county hospitals. It is hoped that the legislature of Pennsylvania now in session and other states will enact a law requiring each county or a group of two or more counties according to size and density of population, to provide an institution for the reception and care of the advanced cases of dependents.

In addition to special county hospitals, general hospitals should be urged to set aside a ward or section for those advanced consumptives who constitute such a great risk to their families. Again, additional sanatoria to which early cases should be sent are urgently needed. It is true that the majority of these sufferers have reached the infective stage, so that they do not obtain a cure, as a rule, nor an arrest even of the disease in many cases, in view of the fact that they cannot be maintained indefinitely in these institutions. This is particularly true of private sanatoria for financial reasons.

While, therefore, the sanatorium does not solve the problem of tuberculosis, the discipline afforded and knowledge gained of the protective measures by the patient are both important and useful to him and tend to safeguard the community, during his long battle with the disease. It has been wisely suggested that sanatoria will be more efficient when completed by a social organization of the nature of an employment bureau providing work suitable to this special class of invalid.

Finally, in my view, the various state tuberculosis societies should further a closer understanding and coöperation with the State Departments of Health, the American Red Cross and all organized, civic and professional agencies working toward the greater control of tuberculosis. Without doubt, such allies are, for certain main purposes, indispensably necessary to success.

ARE EATING UTENSILS CARRIERS OF TUBERCLE BACILLI?

H. LONGSTREET TAYLOR

Saint Paul, Minnesota

Our ordinary eating utensils have been pronounced "the major avenue of tuberculosis transmission" (1), which thesis would make many public health measures necessary, especially in public eating houses, if found to be true.

Dearstyne (2) says:

> More and more it becomes evident that carelessly washed dishes and utensils in eating places and at soda fountains are potential disseminators of infections.

Dearstyne's tables show bacterial counts from different utensils. Small quantities of wash water were poured upon agar plates and incubated forty-eight hours at 37.5°C. Coffee mugs and water glasses were found to be the worst offenders. Individual bacterial counts, ranging from 1000 to 890,000, were found in the case of coffee mugs in six restaurants, and one water glass reached a count of 1,200,000.

Dr. Walter Ramsey (3), investigating the clinical thermometers of physicians, found the following startling results:

> The thermometers from which the cultures were taken were those used by the physicians in their daily practice. Most of them, with the exception of the hospital thermometers, were carried in the ordinary case in the pocket.
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> The technique employed was as follows:
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> Culture tubes containing broth were obtained from the laboratory of the Board of Health. The thermometers were stirred in the broth and after incubation the cultures were transferred to agar plates. After proper incubation the colonies were picked out and examined.
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> The results were as follows:
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> Total cultures taken, 82. Of this number, 33 were sterile; 49 contained organisms of various kinds. Streptococci occurred in 13 cultures; staphylococcus albus and citrus, pneumococcus and many of the ordinary mouth microörganisms were found in the positive cultures.

In order to determine whether eating utensils were being properly washed or whether they carried living virulent tuberculosis germs, the following experiments were carried out in public and private tuberculosis institutions in Minnesota.

In the first place, Dr. G. B. Kramer, Pathologist of the City and County Hospital, St. Paul, Minnesota, was kind enough to examine wash-water with which unwashed spoons, taken from the trays of far advanced positive sputum cases, had been rinsed. He was able to find tubercle bacilli on the fist slide stained. Whereupon the Beebe Bacteriological Laboratory was requested to make a thorough study of the spoons in two tuberculosis institutions. They reported as follows:

November 22, 1920.

Dear Dr. Taylor:

We submit herewith a final report upon the work undertaken for you to determine the possibility of transmitting tubercle bacilli from one person to another upon eating utensils.

On July 30, 1920, experiments were begun at Hospital No. 1, as follows:

Eighteen spoons used by patients in the ward devoted to serious "open" cases, were taken from the diet kitchen. These were spoons which had been washed in the manner regularly employed there, i.e., a thorough washing in hot water. With a sterile swab moistened in sterile salt solution both surfaces and the edge of the bowls of six spoons were thoroughly scrubbed and the swab containing the accumulated swabbings of all six spoons was placed in a tube containing 6 cc. of sterile salt solution. This process was repeated so that

TABLE 1

PIG NUMBER	MATERIAL	OUTCOME	CONCLUSION
257	No. 1 clean	Died 8 weeks	No T. B. Negative
117	No. 1 clean	Died 18 days	No T. B. Negative
245	No. 2 clean	Lived and gained	No T. B. Negative
427	No. 2 clean	Lived and gained	No T. B. Negative
240	No. 3 clean	Died 6 weeks	No T. B. Negative
465	No. 3 clean	Died 7 weeks	No T. B. Negative
433	Clean bottle	Lived and gained	No T. B. Negative
237	Clean bottle	Died 7 weeks	No T. B. Negative
441	Dirty bottle	Died 2 months	Pos. T. B. Positive
398	Dirty bottle	Died 1 month	Pos. T. B. Positive
435	No. 1 dirty	Died 6 weeks	Pos. T. B. Positive
269	No. 1 dirty	Lived and gained	No T. B. Negative
431	No. 2 dirty	Lived and gained	No T. B. Negative
432	No. 2 dirty	Died 1 month	No T. B. Negative
448	No. 3 dirty	Died 5 weeks	No T. B. Negative
232	No. 3 dirty	Died 3 weeks	No T. B. Negative

Conclusions: 16 pigs used. 13 negative for T. B. 3 positive for T. B. All positive pigs injected with material from dirty spoons.

we had three test tubes, each containing the washings from six spoons. This swabbing was done with vigor so that all possible dirt and bacteria were removed; greater pressure was employed than would be exerted by the lips of the next user of the spoon.

In order to check up on efficacy of the swabbing, another lot of six clean spoons was placed in a bottle containing 150 cc. sterile physiological salt solution. These were allowed to soak for a few minutes and then were violently shaken.

This identical process was repeated with a like number of spoons removed from the patients' trays at the end of the noon meal.

The swabs were allowed to soak in the test tubes three hours, at the end of which time all possible salt solution was squeezed out of each swab by pressure against the inside of the tube, and the residue in each tube was injected intraperitoneally into two guinea pigs. The 150 cc. salt solution in the two wash bottles used was centrifugated until there was a residue of 4 cc. in each centrifuge tube. Two pigs were injected with the material from each of these bottles.

The results noted in the sixteen guines pigs used in this experiment will be seen in table 1.

On August 3 a similar experiment was undertaken at Hospital No. 2, the procedure being identical except that only clean spoons were used in the wash bottles.

The results in the fourteen pigs of this experiment are to be seen in table 2.

TABLE 2

PIG NUMBER	MATERIAL	OUTCOME	CONCLUSION
107	No. 1 clean	Died 1 month	No T. B. Negative
206	No. 1 clean	Died 2 weeks	No T. B. Negative
213	No. 2 clean	Died 1 month	No T. B. Negative
228	No. 2 clean	Died 1 month	No T. B. Negative
551	No. 3 clean	Lived and gained	No T. B. Negative
571	No. 3 clean	Lived and gained	No T. B. Negative
554	Clean bottle	Lived and gained	No T. B. Negative
568	Clean bottle	Died 1 month	No T. B. Negative
217	No. 1 dirty	Lived and gained	No T. B. Negative
574	No. 1 dirty	Died 2 weeks	No T. B. Negative
224	No. 2 dirty	Died 5 weeks	Pos. T. B. Positive
221	No. 2 dirty	Died 6 weeks	Neg. T. B. Negative
204	No. 3 dirty	Lived and gained	Neg. T. B. Negative
212	No. 3 dirty	Lived and gained	Neg. T. B. Negative

Conclusions: Fourteen pigs used. 13 negative for T. B. 1 positive T. B. Only positive pig was injected with material from dirty spoon.

TABLE 3

Total pigs used	30 or 100 per cent
Total pigs positive for T. B	4 or 13⅓ per cent
Total pigs negative for T. B	26 or 86⅔ per cent

TABLE 4

Pigs injected with material from clean spoons	16 or 100 per cent
Number of above positive for T. B	0 or 0 per cent
Number of above negative for T. B	16 or 100 per cent

TABLE 5

Pigs injected with material from dirty spoons	14 or	100 per cent
Number of above positive for T. B	4 or	28.5 per cent
Number of above negative for T. B.	10 or	71.5 per cent

From the above tables it will be seen that no pig injected with material from washed spoons contracted tuberculosis. Only in the pigs injected with the wash water from spoons taken directly from the trays of open tuberculous patients were tuberculous lesions found. We would conclude, therefore, that tubercle bacilli are present on spoons used by tuberculous patients, but that the routine washing of such spoons as carried out in these two institutions eliminates these articles as sources of infection.

Very truly yours,
Beebe Laboratories,
By L. L. Gilman.

Dr. F. F. Callahan also examined spoons in a tuberculosis institution. He reports as follows, under date of March 2, 1921:

On August 2, 1920, eight spoons were taken from active cases of pulmonary tuberculosis whose sputum contained many tubercle bacilli. The spoons were washed in hot soapy water in the dishwasher and dried in the usual way. They were then allowed to soak for half an hour in a container with enough sterile distilled water to cover the bowls of the spoons. The whole was then shaken for half an hour. The water was poured off and centrifuged for another half hour.

Ten guinea pigs were injected intraperitoneally with the residue, each pig receiving 1 cc. One pig died at the end of six weeks and another in eight weeks; neither showed any evidence of tuberculosis at necropsy. The remaining eight pigs have continued to grow and gain weight.

The total number of pigs injected in the above experiments was 40, of which number 4 or 10 per cent were infected with tuberculosis. All of these pigs were injected with washings from unwashed spoons.

Not a pig developed tuberculosis that was injected with the washings from spoons that had gone through the usual dish washing of the respective institutions.

Two of the institutions employ dish washing machines with hot water and live steam. In the third one the dishes are washed by patients who are able to be on exercise and who are delegated to wash dishes after one of the daily meals. The dishes are washed in dishpans in the diet kitchen, one of which serves each ward. Hot water is supplied in liberal quantities.

The positive cases show that tubercle bacilli are transferred to eating utensils and that they are potentially exceedingly dangerous avenues of contagion.

Dearstyne's observations show that drinking glasses are fully as dangerous and probably more so, since they offer a larger surface to the lips.

Sanatoria for consumptives should pay special attention to the disinfection of all eating and drinking utensils.

Visiting nurses employed in the care of consumptives in the home should insist on separate eating and drinking utensils for the patient or on the sterilization of all the family dishes after every meal.

Public health officials should enforce the necessary use of steam and hot water in all hotels, restaurants, and soda fountains. These public eating and drinking places must, to a certain degree, be responsible for the dissemination of all infectious diseases of the air passages and lungs and of other constitutional and general diseases.

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HYPERTROPHIC OSTEOARTHROPATHY IN PULMONARY TUBERCULOSIS

A SURVEY OF A SANATORIUM GROUP OF PATIENTS

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Tuberculosis is known to produce certain associated pathological alterations which are manifested in a variety of ways besides producing the essential primary pathological changes of the disease. These secondary changes appear to become more pronounced as the disease progresses and seem to be somewhat related to the duration or activity of the actual primary tuberculous disease condition. On account of the chronicity of tuberculosis the form of the actual gross appearances of these concomitant conditions is at times of a variegated nature. Of these associated concomitant conditions there has been probably most attention paid to the clubbing of the fingers, Pierre Marie's syndrome of *pulmonary hypertrophic osteoarthropathy* or *secondary osteoarthropathy*. The coincident clubbing of the toes, though studied, has been given far less consideration. Likewise, and especially in consumptives, the finger and toe nails have attracted little attention. It is not the purpose of this paper to dwell in detail upon the fundamental histological basis of these tissue changes as observed in tuberculous individuals, a field that pertains more to the realm of the dermatologist, but merely to report the results of a survey of the hands and feet, and oral and facial regions of a group of tuberculosis sanatorium patients, with the view of bringing out some heretofore neglected, or only slightly emphasized, and possibly new facts of interest to tuberculosis and sanatorium physicians.

The literature on clubbed fingers and secondary osteoarthropathy is replete with reports of individual cases, is so voluminous and has been so well summarized by other authors of recent years that only the more important points brought out by these studies will be touched upon here.

In an interesting summary on pathological conditions of the nails, S. Parkes Weber (1) states that

> Incurved nails in wasting diseases need not be associated with clubbing of the finger tips, but clubbing of the finger tips is always associated with more or less incurving or aduncation (hooking) of the nails. The condition is frequently, but by no means always, accompanied by clubbing of the toes; but in such cases the clubbing of the toes is generally less marked than in the fingers. The causes of the clubbing are still not completely understood, but toxic conditions connected with suppuration, etc., and chronic venous congestion and cyanosis (local or general) play important parts in the pathogeny. . . . . A somewhat acute development of clubbed fingers is occasionally observed in pulmonary and other intrathoracic diseases associated with suppuration, such as bronchiectasis, empyema and pulmonary abscess, which need not be accompanied by a considerable cyanosis. . . . . The condition may certainly disappear almost as readily as it arises when it is connected with some curable suppurative condition in the thorax. Occasionally clubbing may develop even within a single week when it is accompanied by pain, while at times no cause could be found for the occurrence of the clubbing.

White (2) in a clinical study of 485 cases of nail disease, collected at the Massachusetts General Hospital over a period of three years, found that eczema (107 cases) produces the most frequent examples of nail disease, trauma or felon (72 cases) being second, paronychia (68 cases) third, psoriasis (67 cases) fourth, and professional dermatitis without paronychia (62 cases) fifth, while syphilis formed only 5 per cent of his cases. There were only 2 cases of tuberculosis verrucosa (vertical ridge, discoloration, separation from bed and broken nail) and only 1 of pulmonary tuberculosis (with increased convexity) revealing nail disease.

In 1890 Pierre Marie (3) first described the skeletal disease characterized by a thickening of the long bones in the vicinity of the joints, with a peculiar clubbing of the finger ends, under the title of *de l'osteo-arthropathie hypertrophiante pneumique* as differentiated from acromegaly. Because of the secondary relation of the disease to some pulmonary affection he appended the adjective *pneumique*. Independently and almost simultaneously (1889 and 1891) Bamberger (4) reported a series of similar cases and called attention to the presence of hippocratic fingers in individuals with bronchiectasis without tuberculosis. Since these original papers numerous reports have been published, more definitely establishing this morbid condition as a distinct clinical entity among the general group of allied diseases, including leontiasis ossae, osteitis deformans, acromegaly, rickets, syphilis of the bones, etc. In a most excellent review and contribution to the study of this subject, Locke (5) of Boston in 1915 added considerable information to our then rather scattered knowledge of this condition. He stated that

> The evidence is overwhelming that hypertrophic osteoarthropathy is always a secondary disease. Among the primary diseases, pulmonary tuberculosis is probably the most important, though rarely inducing the extreme degree of bone and joint changes seen with bronchiectasis. There is a very definite correspondence between the characteristic clinical course of the disease and the process in the bones. During the periods of exacerbation in the primary disease, the pain, tenderness and swelling in the soft parts are not only increased, but the process in the bones is also more active. On the other hand during the quiescent periods associated with cure or relief of the condition responsible for the bone and joint changes, the process in the bones is stationary and in rare instances actual resorption takes place.
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> The new subperiosteal bone, which is at first sharply marked off from the old shaft, later becomes (usually after a period of some years) a more compact, dense layer, closely fused with the underlying old bone. In the late stages of the most progressive type of cases there is evidence of widespread halisteresis in the affected long bones. Occasionally the process in the bones and joints once established may progress even after actual cure of the primary disease. The ungual phalanges as a rule show proliferative changes. They consist mainly in an irregular burr-like expansion of the distal half. More rarely small osteophytes are found at the proximal ends near the line of the joint cartilage. The epiphyses of the affected long bones are to some extent always involved, but the new osseous tissue is much more irregular in outline and the ossification is less complete. The proliferation in the long bones in advanced cases is more general than has been recognized, often affecting nearly the entire skeleton. Changes in the joints are a constant and important feature of the disease. While the early changes are confined largely to the periarticular tissues, in the later stage, erosion of the cartilage, lipping about the joint, and even a moderate degree of ankylosis are common lesions.
>
> A considerable percentage of cases of so called hippocratic fingers show by means of skiagrams early proliferative changes in the periosteum of some of the long bones of the forearms and lower legs of exactly the same type as seen in hypertrophic osteoarthropathy. Simple clubbing of the fingers and secondary hypertrophic osteoarthropathy should be considered as identical, the former representing an early stage of the latter.

Leo Kessel (6) of New York in 1917 made an extensive study of hypertrophic osteoarthropathy in 32 cases of pulmonary tuberculosis of the second or third stage of the disease. Roentgen examinations were made of the hands, feet, all of the long bones, the bones of the pelvis and in some instances the shoulder girdle and cranial bones. Following the classification of Locke, the 32 patients were divided into three groups: (1) five patients presenting simple well defined clubbing of the fingers without bone changes (3 of these had extensive pulmonary cavitation); (2) seventeen patients showing clubbing of the fingers with bone changes in the phalanges; and (3) ten patients with clubbed fingers and changes in the long bones (6 of these presented the globular nose formation and malar thickening). With the exception of the awkward appearance of the lower arms and legs of 3 of the patients in group 3, these patients disclosed nothing in their physical examination to differentiate them from patients in the other two groups, yet the roentgen ray examination revealed decided differences.

Kessel was unable to establish any relation between the clinical manifestations of the pulmonary disease and the type of osteoarthropathy present. Pronounced evidence of pulmonary tuberculosis may be associated with simple clubbing of the fingers, while less marked manifestations of the pulmonary disease may be accompanied by distinct changes in the long bones. The bone changes, moreover, are not definitely associated with the type or degree of the clinical expression of the pulmonary disease. No deviation from the normal nitrogen and calcium metabolism was obtained in these cases. Kessel concludes as a result of his studies that the degree of clubbing corresponds only in a general way with the radiographic findings; bone changes occur more commonly than is ordinarily supposed in the so called simple clubbed fingers; pronounced changes in the long bones may take place without any clinical signs or symptoms being present; the type of bone change in the various groups is the same, the difference being rather in degree; and hypertrophic osteoarthropathy is present more frequently in pulmonary tuberculosis than the usual clinical examination would permit us to believe.

Montgomery (7) in a contribution on the deep transverse furrowing of the finger nails following local asphyxia, believes that the blue or violet discoloration of this condition is due to a local excess of carbon dioxide in the blood and that this occasions the peculiar deformity of the nails with transverse furrowing. The deformity usually arises long after the condition, a pneumonia, for instance, that gave rise to it. He states that

The nail grows from a slot, which is formed by a fold of the integument. In order to comprehend the relationship of the nail to the general integument, it is necessary to regard the skin as one great gland, faced by a horny covering, secreted or elaborated by itself from its own epithelial cells. Out of invaginations in this vast surface there grow modifications of this horny covering; out of invaginations that are holes, hairs grow; out of invaginations that are slots, nails spring. At the bottom of the nail slot there is no papilla as there is at the bottom of the hair hole or follicle, nor is there one needed. The hair has to grow out a long distance as a free floating cylinder, and, therefore, must have a rich supply of nutriment at its base, to be transmitted up its medulla or richly cellular centre. The nail, on the contrary, is a short, flat plate with very little free projecting edge. It is produced back in the previously mentioned slot, and is slid forward on longitudinal grooves in the nail bed, to which it is tightly adherent, and from which it receives nourishment and undoubtedly also some addition to its under surface. Very little nail substance, however, is produced distal to the lunular surface. Any injury received by the nail while it is in the formative stage, deep in the slot, may deform it, and this deformity is gradually slid forward with the natural growth of the nail, and does not become visible until the nail plate is free from the posterior nail fold. It takes six months for the nail to grow out (which coincides with Heller's estimate of the rate of growth of the nail, about 0.1 mm. a day). In addition to the interest attaching to such deformities as indicating the time when the malady that produced them occurred, they also may give some idea of the severity of this malady.

He believes that it also gives some idea of the tenesmic convulsions of the tissues in their effort to expel the carbon dioxide and probably also the accompanying lactic and other acids, that should be carried away by the blood as formed. The process may be a tenesmus of the muscular walls of the blood vessels, comparable to the tenesmus in the muscular walls of the intestine or bladder when these viscera become overfull of expellable contents. The basis for his conception is that given by Yandell Henderson, from which it appears that carbon dioxide is the normal stimulant that supports the circulation, respiration, intestinal tonus and peristalsis, and it is only a step between the normal tonus and spasmodic contraction.

Herbert French (8) in 1917 expressed the opinion that whereas longitudinal (lateral) ridges on nails generally mean nothing in particular, transverse ridges on nails (especially symmetrical) are important evidence of a previous disease, the time and duration of which can be approximated by the transverse ridging. Ball and Alamartine (9) in 1912 express the opinion that hypertrophic osteoarthropathy is occasioned by toxins or poisons developed as a result of pulmonary tuberculosis which, like the urates in gout, have a specific predilection for certain tissues and locations, the changes in hypertrophic osteoarthropathy occurring in spite of the total absence of the tubercle bacilli in these tissues. They describe (10) a condition in dogs similar to that in man and with a like etiology.

The investigations to be reported here were begun with the primary object of studying the nails of the feet of consumptives, in order to determine how many could be benefited by treatment. It had been observed previously that a fairly high percentage of sanatorium patients complained of nail trouble, especially ingrown nails. Upon closer investigation this proved to be in the majority of cases occasioned by the variously called "hippocratic nail" or "parrot beak nail" or "inverted nail" of different authors, associated with hypertrophic osteoarthropathy. As a result of our studies we prefer to call this the *hyperconvex nail of hypertrophic osteoarthropathy*, a more appropriate and descriptive term for this condition.

It was soon realized, however, that if the study were confined merely to the nails, a number of important points valuable in considering treatment might easily be overlooked. It was, therefore, decided to elaborate, and study the hands and feet of a fairly large series of cases of pulmonary tuberculosis. The results of these investigations proved of so much interest that it was decided to further extend these studies.

The oral and facial regions seemed to offer special opportunities. It was in this way that a peculiar nodular tumor was noted upon the hard palate in the midline and extending to the junction of the hard and soft palate. This tumor was especially pronounced in some cases of pulmonary tuberculosis. The condition caused no especial symptomatology and had not even been observed by the patient, except in one or two cases, where it was believed that a gradual increase in size was noted together with a slight change in speech occasioned by the growing tumor. A survey of the literature and consultation with laryngologists did not reveal the identity of this condition, although it had been seen (11) but not correlated with any other condition.

The nails of both the hands and feet of many cases of pulmonary tuberculosis become inverted in the lateral grooves. The nails of the feet cause local pain by pressure, which leads to the impression that the nails are ingrown; but further examination will reveal that the nail edge is merely curved under upon itself and does not enter the flesh as is the case in ingrown nails. The ingrown nail, a normal nail, is occasioned by a true mechanical condition, due to anterior and lateral pressure upon the toe by short shoes or stockings, and differs from the hyperconvex nail, which is a truly pathological nail, attaining its shape as a result of a possible pressure from underneath due to a broadening of the toe as a result of soft tissue and bony changes, but mainly as a result of its changed consistency resulting from disease. Hyperconvex nails are brittle, often with yellow streaks at the bed made up of a soft "caseous" material. The chalky excretion under the nail and in the nail groove, when present, is dry and white and easily pulverized. These nails usually reveal accentuated lateral ridging which is especially noticeable on the hands, while there is also a decided transverse ridging which occurs in waves and more especially to be seen on the feet. The multiple transverse ridges in the consumptive may in some way be related to the periodicity of the disease. Mixed ridging, both lateral and transverse, is usually only found in the large toe nails, but may be present in all toes: it is rare, however, in the finger nails.

The soft tissue manifestations of hypertrophic osteoarthropathy are mainly seen in the distinct broadening of the distal ends of the fingers and toes. They are aptly described by the terms drumstick or clubbed fingers or toes. The nails are either spread broadly over the clubbed ends of the fingers or toes or are markedly inverted on the lateral edges as a result of their softer consistence. The anterior-posterior curvature is markedly increased in convexity and is aptly described as hyperconvex. There may be an involvement of the soft tissues and nails of individual fingers of one hand or foot without symmetrical involvement on the other side. This is commonly seen. There may also be a marked involvement of the soft tissues of the tips of the fingers or toes, with practically normal nails and vice versa. In many cases there is a broadening of the soft tissues in the vicinity of the proximal phalanges of the hands; whether this is due to bony thickening or actual soft tissue increase in this vicinity could not be determined. On account of the deformity frequently occasioned by the wearing of short and narrow shoes which may produce more or less clubbing of the soft tissues of the toes, it is advisable, except in pronounced cases, to forego conclusions until a complete examination of the hands and feet has been made. In the roentgenograph, however, a differentiation is easily made by the disclosure of obliteration of the interphalangeal joints in these cases. (See figure 20.)

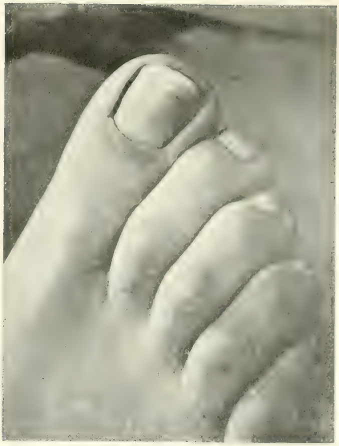

Fig. 1

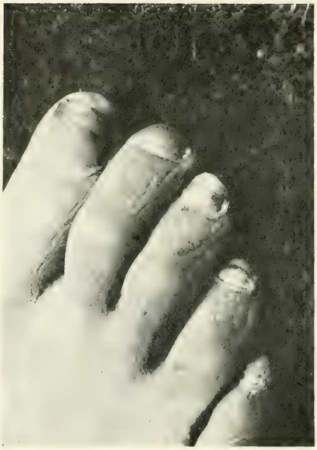

Fig. 2

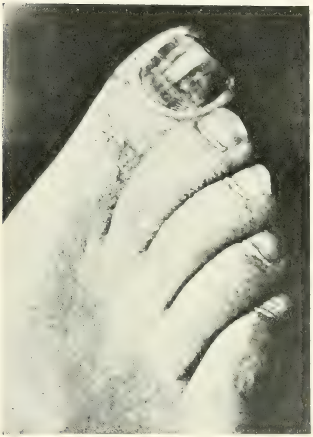

Fig. 3

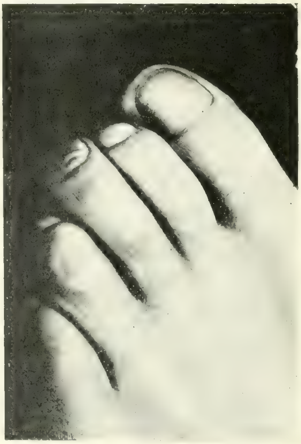

Fig. 4

Fig. 1. Pronounced Lateral Ridging of Nail of Great Toe with Yellow Caseous Excretions under Ridges and Clubbing of Toes

Fig. 2. Pronounced Transverse Ridging of All Toe Nails

Fig. 3. Marked Mixed Ridging of Great Toe in Case of Eczema and Pulmonary Tuberculosis, with Chalky Excretion under Nail. Marked Transverse Ridging of Nail of Small Toe

Fig. 4. Hyperconvex Nails with Mixed Ridging and Clubbing of 3rd and 4th Toes Especially Pronounced

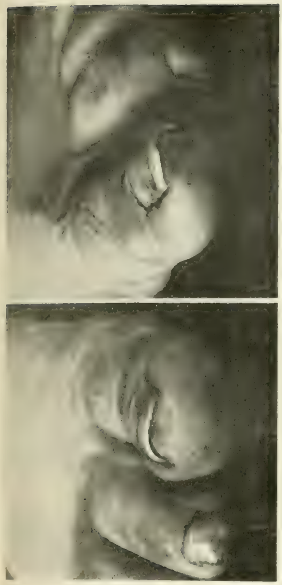

Fig. 6

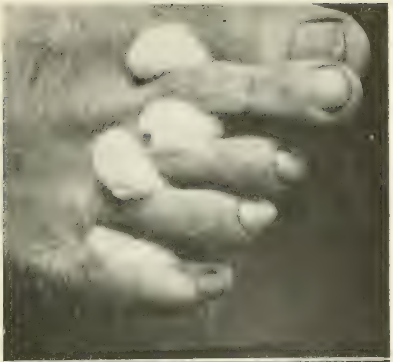

Fig. 8b

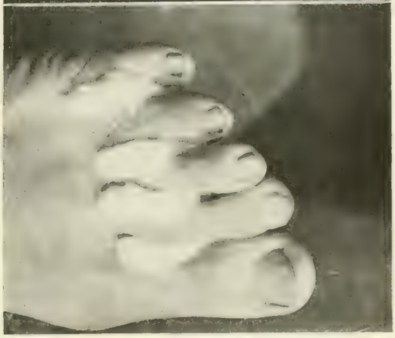

Fig. 8a

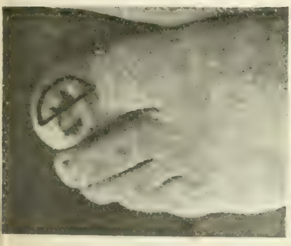

Fig. 5

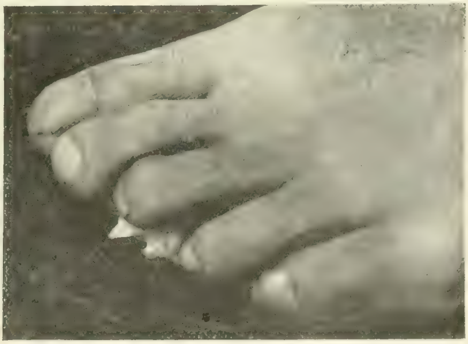

Fig. 7

Fig. 5. Typical Ingrown Nail

Fig. 6. Typical Inverted Toe Nails of Pronounced Type, Showing the Curving under of the Lateral Edges

Fig. 7. Hyperconvexity of All Toe Nails with Lateral Spreading of Nails over the Clubbed Toes

Fig. 8 A. Left Foot with Clubbing of All Toes and Hyperconvexity of the Nails

Fig. 8 B. Right Foot with Same Condition as Fig. 8 A

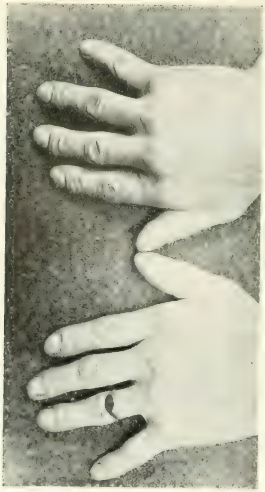

Fig. 10

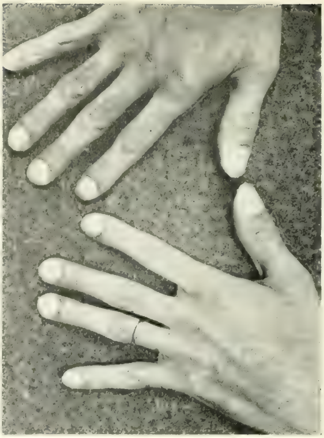

Fig. 12

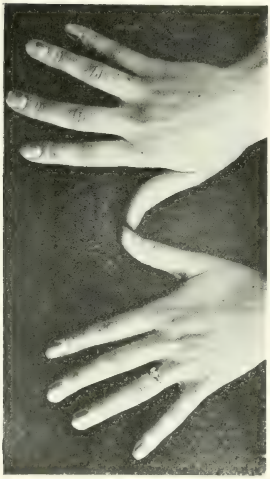

Fig. 9

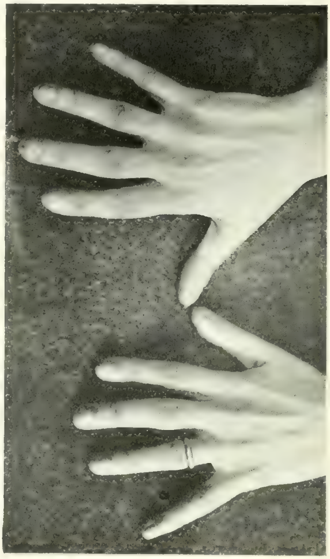

Fig. 11

Fig. 9. Pronounced Lateral Ridging of Finger Nails with Chalky Deposits under the Ridges

Fig. 10. Hyperconvex Nails and Clubbed Fingers with Lateral Spreading of Nails

Fig. 11. Thickening of Distal Phalanx of 1st and 2nd Fingers and Hyperconvexity of the Thumb Nail of the Right Hand

Fig. 12. Clubbed Fingers with Hyperconvex Broad Type of Nails

There may be a hypertrophic condition of the soft tissues of the tips of the fingers and toes without any bony changes and vice versa, corroborating Kessel's findings in this respect. Hypertrophic osteoarthropathy of the bony structures of the hands and feet is manifested most in the burring of the distal ends of the terminal phalanges, which is a prominent factor in the production of the clubbed or drumstick fingers or toes. The periosteal thickening of the phalanges, especially in the proximal phalanx of the finger and the middle phalanx of the toe, is the next most common finding, while involvement of the metatarsals and metacarpals is less frequent. Often heavy spurs may be found at the proximal end of the terminal phalanges of the large toe. Rarely, irregular new bone growth may be seen along the shaft of this phalanx. In some of the more pronounced cases of hypertrophic osteoarthropathy the proximal phalanges of the large toes may lose their concave sides and tend toward a cylindrical form with straight sides. Like the soft tissue changes, the bony manifestations may be irregular, involving single toes, and unsymmetrically the hands and feet. In the hands, when only one or two fingers are involved, the bony changes are more pronounced, usually in the middle finger, while in the feet the second toe is most involved.

These studies revealed that other foot conditions, not directly related to hypertrophic osteoarthropathy, such as flat feet, are due rather to occupational conditions than to this disease, and the percentage among consumptives is not greater than among a group of nontuberculous individuals. Acute and chronic foot strain was not found in the sanatorium group of patients, since the ordinary rest treatment corrects this condition.

Calluses and corns were found distinctly less frequent among this class of patients for the same reason. The complaints of ingrown nails in consumptives taking the rest treatment proved upon examination not to be true ingrown nails, but the incurved nails of the hyperconvex type and not burrowing into the flesh of the lateral grooves of the toes. Hyperhydrosis is not more common in a sanatorium group of consumptives than among a like group of healthy individuals.

In order to obtain information on the incidence of the various manifestations of hypertrophic osteoarthropathy, affecting the hands and feet of consumptives in various stages of the disease and classified according to the activity and approximate duration of the pulmonary condition, the hands and feet of 102 cases of pulmonary tuberculosis patients in the National Jewish Hospital for Consumptives, were carefully examined.

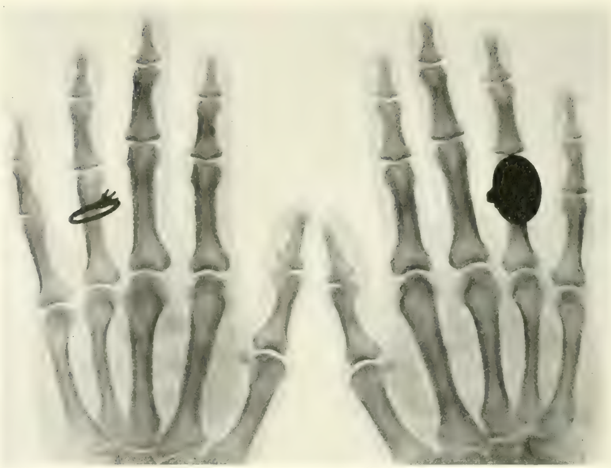

Fig. 13. Skiagraph of Normal Hands

Note the fine pointing of the distal ends and the absence of roughening of the periosteum of the phalanges.

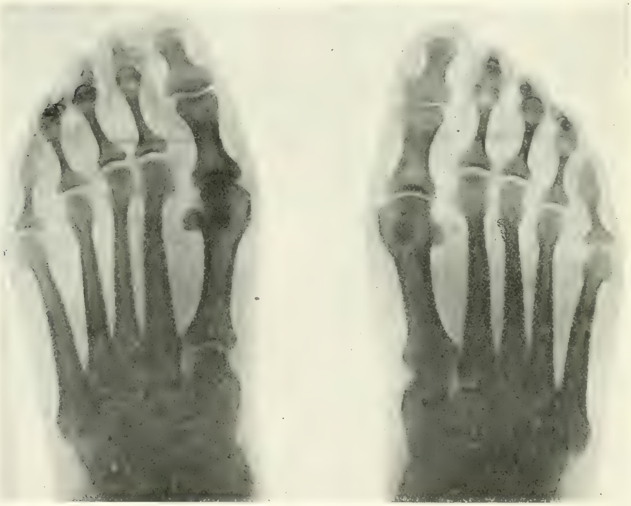

Fig. 14. Skiagraph of Normal Feet

Note the absence of burring on the distal phalanges and the graceful concavity of the shafts (periosteum) of the proximal phalanges.

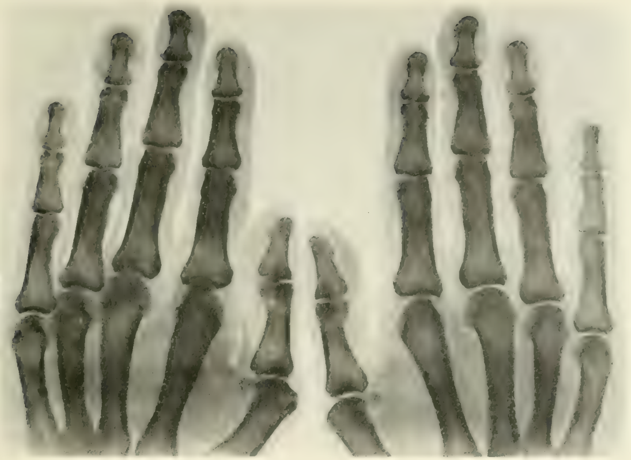

Fig. 15. Skiagraph of Clubbed Fingers

Note burring with spurs on the distal phalanges and thickening of the soft tissues at the distal ends of the fingers.

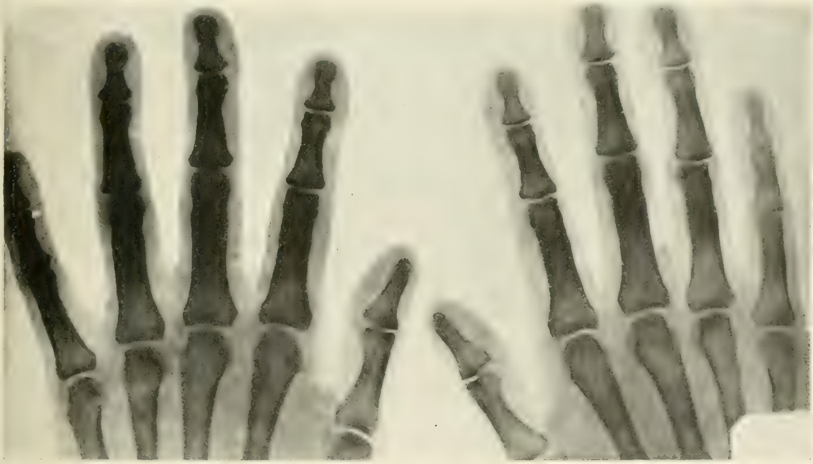

Fig. 16. Skiagraph of Clubbed Fingers

Note marked periosteal thickening of the proximal phalanges and soft tissue thickening of the distal ends of the fingers with burring of the tips of the distal phalanges.

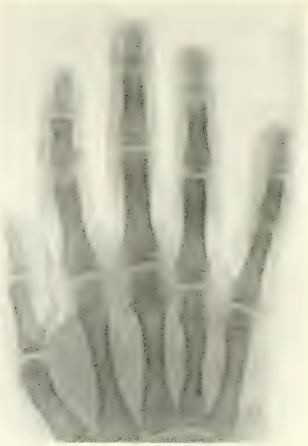

Fig. 17A

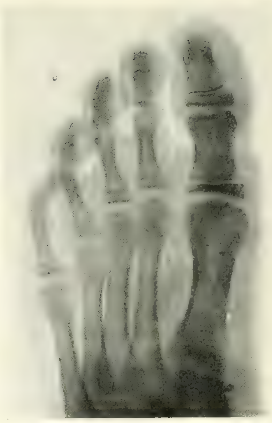

Fig. 17B

Fig. 17 A. Skiagraph of Hand of a Boy with Tuberculosis of the Knee for about Eight Years

Note periosteal thickening of all carpal and phalangeal bones and clubbing of distal phalanges.

Fig. 17 B. Skiagraph of Foot of Nontuberculous Leg of Patient of Fig. 17 A

Note periosteal thickening along shafts of phalanges and metatarsals and extreme width of proximal phalanx of great toe.

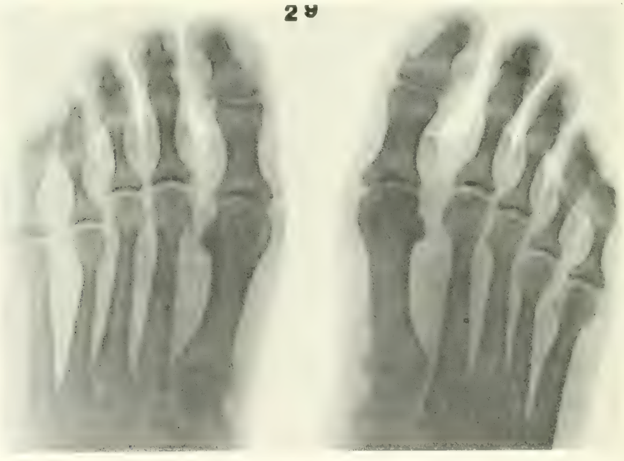

Fig. 18. Skiagraph of Clubbed Toes

Note extreme burring of tips of distal phalanges of all toes except great toe, which has definite spurs on base of distal phalanx. The soft tissues of the ends of all toes are clubbed.

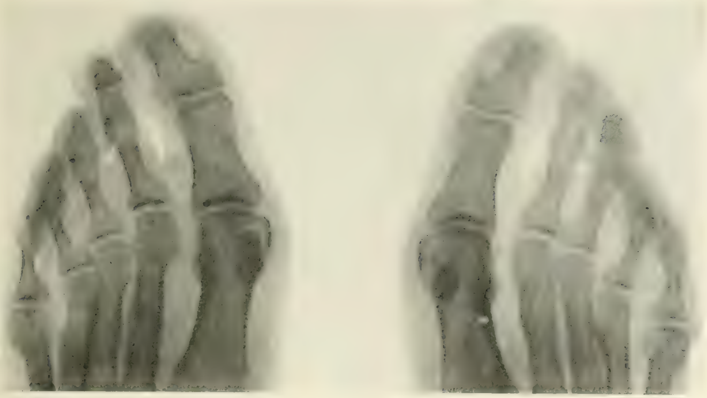

Fig. 19. Skiagraph of Feet

Note irregular bone formation along shafts of metatarsals, thickening of middle phalanges of 2nd and 3rd toes of both feet with obliteration of the concavity, and periosteal thickening of all the bones. The toes are clubbed, with burring of the distal phalanges.

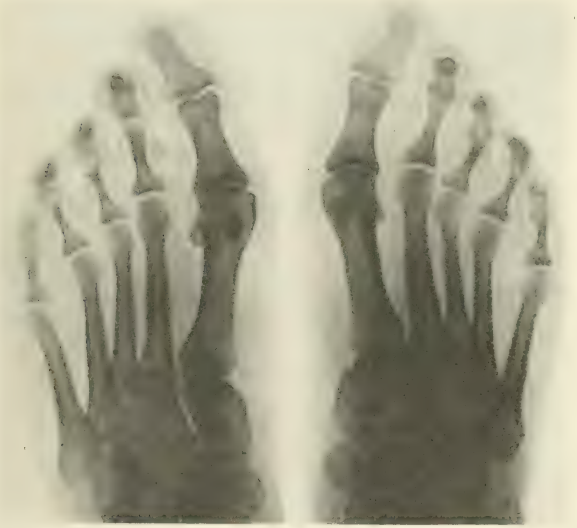

Fig. 20. Skiagraph of a Normal Foot with Slight Clubbing (not Hypertrophic Osteoarthropathy)

Note clubbing of soft tissues of ends of toes and joint obliteration between the 2nd, 3rd and 4th toes of the right foot and of the 2nd and 3rd phalanges of the 4th toe of the left foot, occasioned by wearing short and narrow shoes.

The examination consisted of a careful study of the nails for the type and ridging, and of the soft tissues for clubbing, while the bone changes were studied in roentgenographs. The cases were classified as carefully as possible into the various stages of the disease, the presence of activity and the approximate duration of the disease and tabulated with the results given in tables 1 and 2. For comparison a series of 12 normal individuals were also studied with the results incorporated in table 1. The cases were further classified into males and females except in the incipient class, where the number of cases (7) was too few to permit of such division satisfactorily.

Tables 1 and 2 bring out the following points:

1. In consumptives there is found a high percentage of hyperconvex nails regardless of the stage of the disease. The incidence on the hands is exactly the same as that on the feet.

2. Lateral ridging of the finger nails is present to a slight extent in normal individuals and is merely accentuated in the consumptive. The same condition exists in the feet, where, however, slight transverse ridging is found fairly often in normal individuals. In the consumptive the ridging of the toe nails of the feet becomes more marked, and pronounced transverse and mixed ridging is much more frequent. (In the tabulation these points could not be brought out.)

3. Hypertrophy of the soft tissues of the hands, especially to be seen at the tips of the fingers and thumb, is practically absent in normal individuals (unless produced by mechanical and occupational means, when it may be slight and the cause discovered by a complete examination), and is common among consumptives. This is also the case in hypertrophy of the soft tissues of the toes, seen most pronounced at the tip, being common among consumptives. The incidence of soft tissue hypertrophy is about the same in the toes and in the fingers of cases of pulmonary tuberculosis. The incidence of soft tissue hypertrophy is greater in the active than in the inactive cases of pulmonary tuberculosis.

4. The incidence of bone hypertrophy of the hands and feet, especially to be seen as burring of the tips of the distal phalanges and periosteal thickening of the shafts of the phalanges and the metacarpal and metatarsal bones, may be present to a slight extent in "so called" normal individuals (as seen in two cases having had an acute pulmonary infection (influenza) a short time prior to the examination) but is common to a pronounced degree among consumptives. The incidence of bone hypertrophy is about the same in the toes and in the fingers of cases

of pulmonary tuberculosis. The incidence of bone hypertrophy is greater in the active than in the inactive cases of pulmonary tuberculosis.

5. No significant differences in the incidence of the manifestations of hypertrophic osteoarthropathy in cases of pulmonary tuberculosis were noted, whether the pulmonary condition had been of short (one year or under) or long (over three years) duration.

A result of the study of the literature and Kessel's findings of malar thickening and globular nose formation, especially in the more pronounced cases of hypertrophic osteoarthropathy in consumptives, led to the belief that the hypertrophic condition was generalized, and that further study of regions heretofore unobserved, that is, the facial and oral regions would lead to interesting findings. It seemed highly probable that the jaws might reveal something of significance. In this study of the oral and facial regions there were included 94 cases of pulmonary tuberculosis of various stages (National Association Classification), and for comparison 12 normal individuals. The studies were divided into careful observations of the teeth, gums, bony processes of the jaw, hard and soft palate, tongue, nose, and malar processes. Roentgenological study was made in a number of these cases, but on account of the difficulty of interpretation it revealed nothing of special significance and was discontinued. The cases were classified according to sex, activity and duration of disease. The results are given in tables 3 and 4.

In the adult consumptive (contracting the disease after early childhood) the teeth revealed nothing of significance or possible of interpretation. In some cases the roots seemed to be more bulbous but whether this had anything to do with hypertrophic osteoarthropathy could not be determined. As a whole the consumptive does not differ in structural tooth conditions from the normal individual. In children with tuberculosis the incisors were serrate, and the crowns of the bicuspids and molars were irregular, and tooth decay was more prevalent than normal, being almost coincident with eruption of the teeth.

Pyorrhoea alveolaris is common among consumptives both young and adult. The gums of the consumptive are in the majority of cases anemic and hypertrophied and do not bleed readily. Upon extracting teeth the socket is dry and does not bleed readily but seems to heal rapidly. The bony processes in a great many cases reveal a decided thickening, TABLE

Hyperthropic osteoarthropathy affecting the hands and feet of consumptives in various stages of the disease classified according to activity

STAGE OF DISEASE	NUMBER OF CASES	ACTIVITY	FINDINGS	NAILS				HYPERTROPHIC OSTEOARTHROPATHY			
				Type		Ridging		Soft tissue changes		Bone changes	
				Hands	Feet	Hands	Feet	Hands	Feet	Hands	Feet
Normals, male and female	12		+	0	0	12 lat.	10 lat. 2 trans.	0	0	2*	2*
			−	12	12	0	0	12	12	10	10
Incipient	7, 4 males, 3 females	+2	+	2	2	2 lat.	2 trans.	1	1	1	1
			−	0	0	0	0	1	1	1	1
		−5	+	5	5	5 lat.	5 trans.	1	3	3	4
			−	0	0	0	0	4	2	2	1
Moderately advanced	20, males	+6	+	5	5	6 lat.	3 lat. 22 mixed 1 trans.	5	5	6	6
			−	1	1	0	0	1	1	0	0
		−14	+	13	13	14 lat.	4 lat. 8 trans. 2 mixed	6	9	8	7
			−	1	1	0	0	8	5	6	7
	9, females	+3	+	3	3	3 lat.	2 lat. 1 trans.	3	3	2	3
			−	0	0	0	0	0	0	1	0
		−6	+	4	4	5 lat. 1 trans.	4 lat. 2 trans.	2	3	1	1
			−	2	2	0	0	4	3	5	5

Far advanced	42, males	+36	+	29	29	36 lat.	23 lat. 6 mixed 7 trans.	28	31	33	31
			−	7	7	0	0	8	5	3	5
		−6	+	6	6	6 lat.	3 lat. 3 trans.	3	1	3	2
			−	0	0	0	0	3	5	3	4
	24, females	+24	+	20	20	22 lat. 2 trans.	21 lat. 3 trans.	15	16	10	8
			−	4	4	0	0	9	8	14	16

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* These changes were slight but definite, and in these 2 cases a history of a severe influenza was obtained.

TABLE 2

Hypertrophic osteoarthropathy affecting the hands and feet of consumptives classified according to the duration of the disease

STAGE OF DISEASE	NUMBER OF CASES	DURATION OF DISEASE	FINDINGS	NAILS				HYPERTROPHIC OSTEOARTHROPATHY			
				Type		Ridging		Soft tissue changes		Bone changes	
				Hands	Feet	Hands	Feet	Hands	Feet	Hands	Feet
Incipient	7, 4 males, 3 females	1 yr. or under (2)	+	2	2	2 lat.	2 trans.	0	1	2	2
			–	0	0	0	0	2	1	0	0
		1–3 yrs. (4)	+	4	4	4 lat.	4 trans.	1	2	1	2
			–	0	0	0	0	3	2	3	2
		Over 3 yrs. (1 tb. knee, 8 yrs.*)	+	1	1	1	1 trans.	1	1	1	1
			–	0	0	0	0	0	0	0	0
Moderately advanced	20, males	1 yr. or under (6)	+	6	6	6 lat.	3 lat. 2 trans. 1 mixed	5	5	6	4
			–	0	0	0	0	1	1	0	2
		1–3 yrs. (5)	+	3	3	5 lat.	1 lat. 2 trans. 2 mixed	3	3	3	3
			–	2	2	0	0	2	2	2	2
		Over 3 yrs. (9)	+	9	9	9 lat.	3 lat. 5 trans. 1 mixed	3	6	5	6
			–	0	0	0	0	6	3	4	3

Moderately advanced	9, females	1 yr. or under (1)	+	1	1	1 lat.	1 trans.	0	1	1	1
			–	0	0	0	0	1	0	0	0
		1–3 yrs. (6)	+	6	6	5 lat. 1 trans.	4 lat. 2 trans.	5	5	2	3
			–	0	0	0	0	1	1	4	3
		Over 3 yrs. (2)	+	0	0	2 lat.	2 lat.	0	0	0	0
			–	2	2	0	0	2	2	2	2
Far advanced	42, males	1 yr. or under (4)	+	4	4	4 lat.	3 lat. 1 trans.	3	3	3	3
			–	0	0	0	0	1	1	1	1
		1–3 yrs. (15)	+	10	10	15 lat.	13 lat. 2 mixed	12	11	12	11
			–	5	5	0	0	3	4	3	4
		Over 3 yrs. (23)	+	21	21	23 lat.	10 lat. 9 trans. 4 mixed	16	18	21	19
			–	2	2	0	0	7	5	2	4
	24, females	1 yr. or under (2)	+	1	1	2 lat.	2 lat.	0	1	0	1
			–	1	1	0	0	2	1	2	1
		1–3 yrs. (9)	+	8	8	7 lat. 2 trans.	8 lat. 1 trans.	7	7	6	3
			–	1	1	0	0	2	2	3	6
		Over 3 yrs. (13)	+	11	11	13 lat.	11 lat. 2 trans.	8	8	4	4
			–	2	2	0	0	5	5	9	9

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* This case is in a boy with only small lung involvement but a tuberculous knee of eight years duration. He is classed as incipient because of the slight lung involvement which seemingly is the significant finding in H. O. A., while in standard N. A. class he would be classed as F. A.

which seems to be more pronounced in the superior maxilla than in the lower jaw or mandible. This reveals itself on the internal surface of the lower jaw, first above a line at the level of the genial tubercle and extending around to about the first molar tooth, obliterating the concavity above this line. The external surface of the lower jaw at about the same level thickens to a lesser degree. On the upper jaw or maxilla the thickening is more pronounced on the external surface following the concavity above the teeth, being more pronounced in the molar region. The internal surface is less involved.

In about 25 per cent of the cases of pulmonary tuberculosis the hard palate reveals a thickening located in the midline and extending from the horizontal plate of the palate bone to the foramen of Scarpa, situated in the anterior portion of the palatal process of the superior maxilla, especially in pronounced cases. The tumor early may only be revealed as a slight elevation in the midline covered by an anemic mucous membrane, and sometimes can only be found by palpation. In the more pronounced cases the tumor situated in the midline is covered with a distinct anemic mucous membrane. The tumor is distinctly hard and bone-like to the touch. Its growth is so gradual that it passes unnoticed by the patient but may cause a slight change in articulation.

Changes in the soft palate were extremely difficult of interpretation and the examinations, therefore, yielded nothing of special interest regarding this part of the palate. Likewise, changes in the tongue were difficult of interpretation, and only decided enlargement of this organ was considered and recorded as abnormal from the standpoint of hypertrophic osteoarthropathy. The same was true in the case of the globular formation of the nose and the thickened malar processes. The figures in these cases are merely given for what they are worth and only indicate a possible deviation from normal.

Tables 3 and 4 bring out the following important points not noted above:

1. In consumptives there is found a high incidence of hypertrophic involvement of the gums which is slightly more pronounced in the active than in the inactive cases. The teeth show nothing of especial significance.

2. Hypertrophy of the bony processes of the jaws (mandible and maxilla) is fairly common in cases of pulmonary tuberculosis, the incidence being greater in the active cases.

TABLE 3

Hypertrophic osteoarthropathy affecting the oral and facial regions in consumptives during various stages of the disease classified according to activity

STAGE OF DISEASE	NUMBER OF CASES	ACTIVITY	FINDINGS	ORAL REGIONS						FACIAL REGIONS	
				Teeth	Gums	Bony processes of jaws	Hard palate	Soft palate	Tongue	Nose	Malar processes
Normal male and female	12		+	0	0	0	0	0	0	0	0
			—	12	12	12	12	12	12	12	12
Incipient	6 (4 males, 2 females)	+1	+	0	1	1	1*	1	0	0	0
			—	1	0	0	0	0	1	1	1
		−5	+	1†	4	4	2	0	1	0	0
			—	4	1	1	3	5	4	5	5
Moderately advanced	18, males	+7	+	0	7	4	2	0	1	0	0
			—	7	0	3	5	7	7	7	7
		−11	+	0	7	0	0	0	0	2	0
			—	11	4	11	11	11	11	9	11
	7, females	+4	+	0	4	1	1	0	0	1	0
			—	4	0	3	3	4	4	3	4
		−3	+	0	1	0	0	0	0	0	0
			—	3	2	3	3	3	3	3	3
Far advanced	48, males	+44	+	1	39	21	10	0	5	7	5
			—	43	5	23	34	44	39	37	39
		−4	+	0	4	1	0	0	0	0	0
			—	4	0	3	4	4	4	4	4
	15, females‡	+15	+	0	13	6	8	0	3	4	1
			—	15	2	9	7	15	12	11	14

* Thickening centre of hard palate.

† Boy with tuberculous knee; incisors irregular and molars soft.

‡ There were no female inactive cases in the far advanced class in this series.

TABLE 4

Hypertrophic osteoarthropathy affecting the oral and facial regions in consumptives classified according to the duration of the disease

STAGE OF DISEASE	NUMBER OF CASES	DURATION OF DISEASE	FINDINGS	ORAL REGIONS						FACIAL REGIONS	
				Teeth	Gums	Bony processes of the jaw	Hard palate	Soft palate	Tongue	Nose	Malar processes
Incipient	6 (4 males, 2 females)	1 yr. or under (2)	+	0	2	2	1	0	0	0	0
			−	2	0	0	1	2	2	2	2
		1–3 yrs. (2)	+	0	1	1	0	0	0	0	0
			−	2	1	1	2	2	2	2	2
		Over 3 yrs. (2)	+	1*	2	2	2	1	1	0	0
			−	1	0	0	0	1	1	2	2
Moderately advanced	18, males	1 yr. or under (2)	+	0	1	0	0	0	0	0	0
			−	2	1	2	2	2	2	2	2
		1–3 yrs. (10)	+	0	8	4	2	0	1	0	0
			−	10	2	6	8	10	9	10	10
		Over 3 yrs. (6)	+	0	5	0	0	0	0	2	0
			−	6	1	6	6	6	6	4	6
	7, females	1 yr. or under (2)	+	0	1	0	0	0	0	0	0
			−	2	1	2	2	2	2	2	2
		1–3 yrs. (5)	+	0	4	1	1	0	0	1	0
			−	5	1	4	4	5	5	4	5
		Over 3 yrs. (0)	+								
			−								
Far advanced	48, males	1 yr. or under (7)	+	1	7	3	1	0	0	2	1
			−	6	0	4	6	7	7	5	6
		1–3 yrs. (16)	+	0	13	7	3	0	2	0	3
			−	16	3	9	13	16	14	16	13
		Over 3 yrs. (25)	+	0	23	12	6	0	3	5	1
			−	25	2	13	19	25	22	20	24
	15, females	1 yr. or under (3)	+	0	3	0	1	0	0	0	0
			−	3	0	3	2	3	3	3	3
		1–3 yrs. (2)	+	0	2	0	1	0	0	1	0
			−	2	0	2	1	2	2	1	2
		Over 3 yrs. (10)	+	0	8	6	6	0	3	3	1
			−	10	2	4	4	10	7	7	9

* Incisor notched and molars decayed.

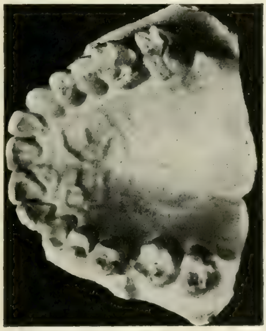

Fig. 21

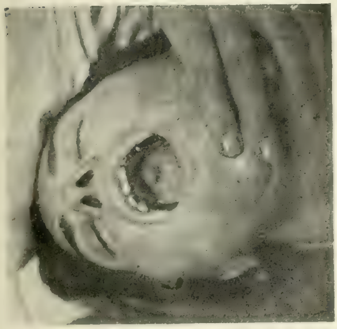

Fig. 22A

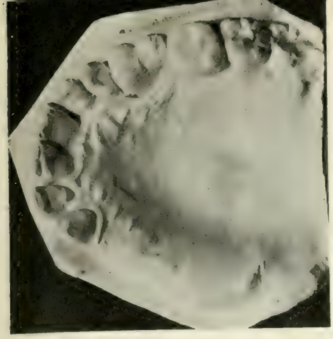

Fig. 22B

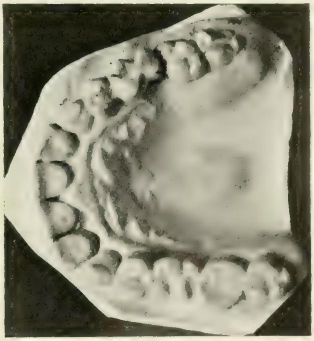

Fig. 23

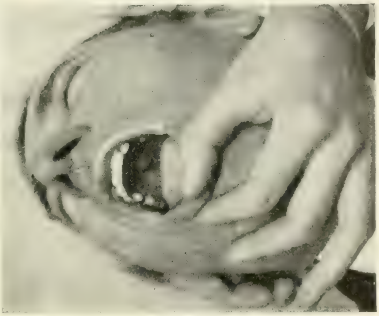

Fig. 24A

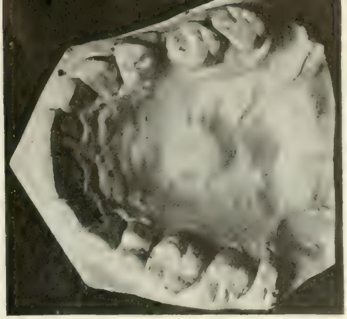

Fig. 24B

Fig. 21. Plaster Model of Normal Roof of Mouth
Fig. 22 A. Photograph, to Show Tumor-Like Nodule of Hard Palate
Fig. 22 B. Plaster Model of Roof of Mouth (Fig. 22 A), to Show Teeth and Hard Palate with Tumor-Like Nodule in Midline
This is a case with slight enlargement
Fig. 23. Plaster Model of Roof of Mouth, to Show Moderate Sized Tumor-Like Nodule in Midline
Fig. 24 A. Photograph, Showing Tumor-Like Nodule of Hard Palate
Fig. 24 B. Plaster Model of Roof of Mouth (Fig. 24 A), Showing Pronounced Nodule in Midline

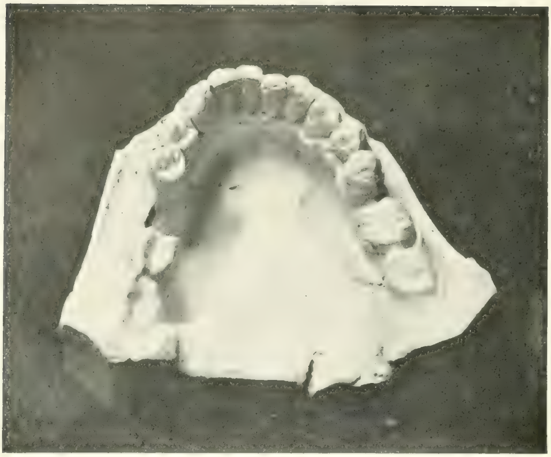

Fig. 25. Plaster Model Showing Normal Inner Plate of the Alveolar Process of the Mandible

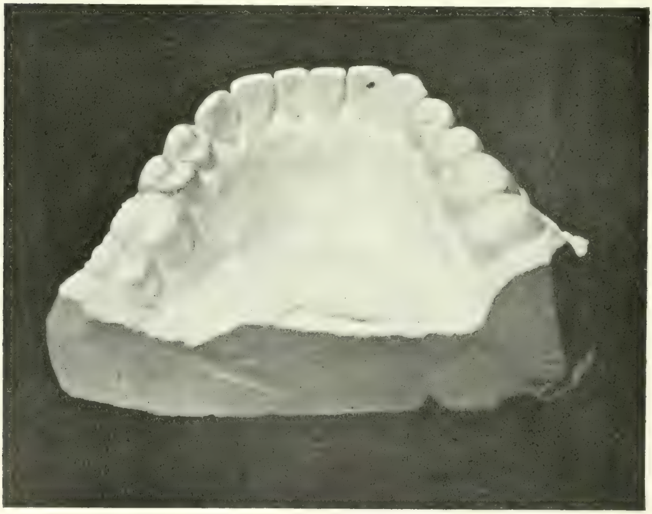

Fig. 26. Plaster Model Showing Enlargement of Inner Plate of Alveolar Process of Mandible, with Obliteration of Normal Concavity

3. Hypertrophy in the midline of the hard palate is fairly common among consumptives, and the incidence is greater in the active cases, which seems to correlate this condition with general hypertrophic osteoarthropathy.

4. There seems to be very little correlation between the above conditions and the actual duration of the pulmonary condition.

5. The condition of the soft palate and tongue could not be correlated with the general condition of hypertrophic osteoarthropathy.

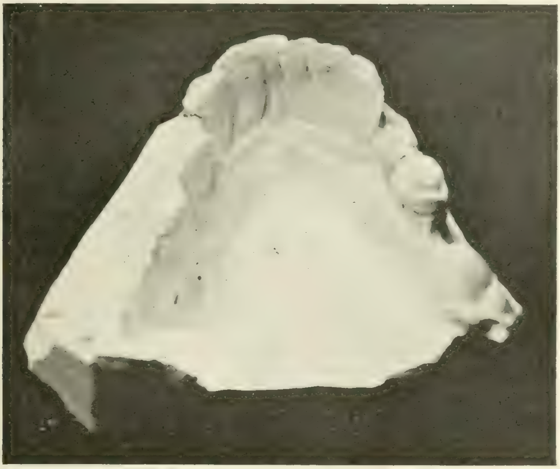

FIG. 27. PLASTER MODEL SHOWING ENLARGEMENT OF INNER PLATE OF ALVEOLAR PROCESS OF MANDIBLE, WITH IRREGULAR HYPERTROPHY IN THE CONCAVITY

6. Although malar thickening and globular formation of the nose was noted, its relation to hypertrophic osteoarthropathy could not be definitely established because of the difficulty in interpreting these conditions in the patients studied.

In order to better interpret the more important hypertrophic involvements of the hands, feet and oral regions two composite tables were made incorporating in percentages the positive findings classified according to sex, and the activity and the duration of the disease, from the previous detailed tables 1 to 4. These figures are given in table 5, classified according to activity, and table 6, classified according to the duration of the disease. These tables give the exact percentage incidence of the various hypertrophic conditions found in the entire group of consumptives studied.

TABLE 5

Composite table of the incidence of the most common manifestations of hypertrophic osteoarthropathy involving the hands, feet and oral regions of consumptives; classified according to the sex and the activity of the disease

SEX	ACTIVITY	NUMBER OF CASES	NAILS	HYPERTROPHIC OSTEOARTHROPATHY				ORAL REGIONS		
				Soft tissue changes		Bone Changes		Gums	Bony processes	Hard palate
				Hands	Feet	Hands	Feet			
			per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
Male	+	43	81	79	86	93	88	90	50	25
	–	23	95	44	52	56	52	73	21	10
Female	+	28	86	64	68	43	40	85	40	45
	–	8	75	25	50	25	38	50	25	25

TABLE 6

Composite table of the incidence of the most common manifestations of hypertrophic osteoarthropathy involving the hands, feet and oral regions of consumptives; classified according to the sex and the duration of the disease

SEX	DURATION OF DISEASE	NUMBER OF CASES	NAILS	HYPERTROPHIC OSTEOARTHROPATHY				ORAL REGIONS		
				Soft tissue changes		Bone changes		Gums	Bony processes	Hard palate
				Hands	Feet	Hands	Feet			
			per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
Male	1 yr. or under	12	100	66	75	91	75	90	46	19
	1–3 yrs.	21	67	76	67	71	71	81	45	19
	Over 3 yrs.	33	94	60	76	81	79	90	40	22
Female	1 yr. or under	4	75	0	50	50	75	80	0	20
	1–3 yrs.	16	94	75	75	50	38	75	13	25
	Over 3 yrs.	16	75	56	56	32	32	81	63	63

Tables 5 and 6 emphasize the following points not discernible from the previous tables:

1. Hyperconvex nails of the hands and feet are found to the extent of about 75 to 95 per cent in cases of pulmonary tuberculosis. The percentage incidence in the active cases does not differ materially from

the percentage incidence in the inactive cases. The incidence in male and female is approximately equal.

2. Hypertrophy of the soft tissues of the hands and feet of male consumptives has a higher percentage incidence in the active cases (about 80 per cent) than in the inactive cases (about 45 per cent). The incidence in females, about 65 per cent in the active cases and 40 per cent in the inactive cases, is slightly lower than in the males.

3. The same holds true for bony changes of the hands and feet of male consumptives (active cases about 90 per cent and inactive cases about 55 per cent) and of female consumptives (active cases about 40 per cent and inactive cases about 30 per cent).

4. Hypertrophy of the gums is approximately of the same incidence in males (active cases about 90 per cent and inactive cases about 75 per cent) and females (active cases about 85 per cent and inactive cases about 50 per cent), although the active cases have a higher incidence than the inactive cases.

5. The same is true of the hypertrophy of the bony processes of the jaws (mandible and maxilla), the incidence being about the same in males (active cases about 50 per cent, inactive about 20 per cent) and females (active cases about 40 per cent and inactive 25 per cent), although the active cases have a somewhat higher incidence in both males and females.

6. The incidence of the tumor-like hypertrophy of the hard palate was slightly more prevalent in females (active cases about 45 per cent and inactive about 25 per cent) than in males (active cases about 25 per cent and inactive about 10 per cent). The incidence in the active cases was also greater than in the inactive cases.

7. No such correlation exists between the incidence of these various manifestations of hypertrophic osteoarthropathy and the approximate duration of the disease, this factor seemingly being insignificant in contradistinction to the significance of the activity of the disease in the incidence of the manifestations of hypertrophic osteoarthropathy of the hands, feet and oral regions of cases of pulmonary tuberculosis (see table 6).

SUMMARY AND CONCLUSIONS

Hypertrophic osteoarthropathy is a common secondary pathological condition in consumptives, manifesting itself as a hypertrophy of the soft tissues and bony structures of the body, with certain sites of predilection. It is probable that there are still many sites in the body which have thus far escaped attention.

The most common sites of the osseous manifestations of this associated pathological alteration in tuberculosis are the distal and proximal phalanges of both the hands and feet, the long bones of the arms and legs (Locke and Kessel), and the bony processes (jaws and hard palate) of the oral cavity.

The most common sites of the soft tissue manifestations are the tips of the distal phalanges of both the hands and feet and possibly to a certain extent the nose and malar processes (Kessel).

The toe nails and finger nails are also a common site of the manifestations of hypertrophic osteoarthropathy, the expressions of this condition of the nail being an increased convexity of the anterior posterior curvature—"the hyperconvex nail"—a lateral broadening, and increased ridging both lateral and transverse.

Hyperconvex nails of the hands and feet of consumptives occurred to the extent of about 75 to 95 per cent in the series studied, there being no difference in the incidence dependent upon the activity of the disease or the sex of the case.

Hypertrophy of the soft tissues of the hands and feet of consumptives has a higher incidence in the active (about 65 to 80 per cent) than in the inactive cases (about 45 per cent).

Bone changes of the hands and feet of consumptives are more common in the active (about 90 per cent in males) than in the inactive cases (about 55 per cent in males). The incidence of bone changes was less in the females than in the males.

Hypertrophy of the bony processes of the jaws in consumptives was greater in the active (about 50 per cent) than in the inactive cases (about 20 per cent).

A tumor-like hypertrophy of the hard palate was found in consumptives, apparently a manifestation of hypertrophic osteoarthropathy, which like the other manifestations of this condition had a greater incidence in the active cases (about 45 per cent in males) than in the inactive cases (about 25 per cent in males).

No significant differences in the incidence of the manifestations of hypertrophic osteoarthropathy in cases of pulmonary tuberculosis were noted, whether the pulmonary condition had been of short (one year) or longer duration (over three years).

A complete study is essential to the diagnosis of hypertrophic osteoarthropathy in consumptives, because of the varied manifestations of this condition and the simulation of the individual symptoms by other conditions, both mechanical and occupational.

A roentgenological study for bone changes in the absence of external findings is essential to the making of a diagnosis of hypertrophic osteoarthropathy, as was pointed out by Kessel.

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THE SURVIVAL AND VIRULENCE OF TUBERCLE BACILLI IN EXCISED ANIMAL LYMPH NODES

FURTHER STUDIES

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About five years ago we began a series of experiments on the production of tuberculosis by transplants of tuberculous lymph nodes and other tissues. The first report on this research was made in 1918 (1), and the main conclusion was as follows: that when tuberculous lymph nodes, or, for comparison, pieces of liver and spleen, are removed from tuberculous guinea pigs, and replanted under the skin in normal animals, and are retained, the bacilli thus transferred invariably produce a general tuberculosis which differs in no apparent way from that which follows inoculation with free virulent bacilli.

Another phase of our earlier experiments dealt with the results of transplanting tuberculous nodes coated with collodion. When these were retained, they showed a progressive shrinkage by diffusion through the collodion membrane into the surrounding tissues of the host, until after several months nothing was left of the original node, of about 1 cm. in diameter, but a minute mass about as big as a split pea, enveloped in a shrivelled collodion skin, and with its centre solidly calcified.

In some cases large caseous collodion-coated nodes were planted in tuberculous animals, and this was followed by local inflammation and acute sickness, suggesting that the substances diffusing through the capsule were toxic for the tuberculous animal. But when the coated nodes were planted in normal animals the procedure was followed by no reaction, no altered sensitiveness to old tuberculin, no evidence of change in resistance to a subsequent tuberculous infection, and no lesions of tuberculosis.

In one instance, after the coated node had been retained for about two months, a small ulcer developed over it. We excised node and skin, and found that the capsule had broken, and there was free communication between its contents and the host's tissues. The pig was kept alive, and remained entirely free from disease, as did another pig inoculated with pus from the excised lesion. This suggested that the bacilli did not remain alive in these coated nodes (2), as Heymans (3) has stated that they do when planted as an emulsion in pith capsules. Following this lead, we coated several nodes and kept them in normal salt solution in the incubator, then after a few weeks we inoculated fresh pigs with the contents. These pigs also remained free from tuberculosis.

It now became necessary to determine whether there was something in the process of coating the nodes which killed the bacilli. We therefore undertook similar experiments with uncoated nodes. Guinea pigs were inoculated subcutaneously with virulent human tubercle bacilli, and when their inguinal nodes were grossly tuberculous the pigs were killed, and the nodes excised and placed in tubes of sterile salt solution in the incubator. At the same time an emulsion of tubercle bacilli was prepared in an exactly similar tube of salt solution, and placed with the other tubes in the incubator. At progressive intervals of time, nodes were taken out of their tubes and cut in two. One half was planted in a fresh pig, and the other half saved for microscopic sections, especially for examination as to the number and appearance of the tubercle bacilli present. At the same intervals, pigs were inoculated with the emulsion. The pig given a fresh node developed palpable tuberculosis of the inguinal nodes in fifteen days. Those given nodes which had been fifteen, twenty-nine, and forty-three days in the incubator developed no lesions. The pigs inoculated with emulsion which had been kept the same periods of time all became tuberculous in from ten to fifteen days (table 1).

This first outline experiment was followed by another more extensive series, as a result of which we were able to conclude that the bacilli contained in the incubated nodes had completely lost all power to infect in seven days, and that the same change took place in tuberculous liver and spleen in three weeks or less. Experiments with these tissues at shorter time intervals are now in progress, and so far it appears that the results are the same as with the lymph nodes. The emulsion was still virulent after eighty-seven days (table 2). This loss of virulence was apparently due to the death of the bacilli, as cultures made from several of the tissues in question remained sterile, but we do not regard this point as absolutely established. It bore no relation to the presence or absence of contamination in the tubes. Several tubes became contaminated with staphylococci, and some of the nodes from these tubes caused local abscesses when planted, but the results as regards tuberculosis were the same as in the case of the nodes which remained uncontaminated. The nodes themselves are believed to have been in every case free from mixed infection during life.

The loss of virulence was not accompanied by any noticeable changes in the shape or staining reaction of the bacilli, though variations occurred, as they often do in fresh material. Nodes, which had been incubated twenty-one, twenty-three and even forty-three days, showed large numbers of tubercle bacilli staining well with carbol-fuchsin, as appears in the tables, and the histological picture of the tissues themselves showed remarkably little change in this time. Connective tissue, fat tissue, and endothelial cells in many cases were so well preserved that it would be impossible to assert that they were not alive. Lymphocytes were somewhat less durable, and liver cells showed decided changes even at two days.

TABLE 1

GUINEA PIG NUMBER	GIVEN	TIME TISSUE OR EMULSION HAD BEEN IN INCUBATOR	RELATIVE NUMBER OF TUBERCLE BACILLI IN SECTIONS	CONTAMINATION OF TUBE	ABSCESS AFTER PLANT	TUBERCULOSIS OF HOST'S INGUINAL NODES FIRST NOTED	TIME ELAPSED BETWEEN PLANT OR INOCULATION AND AUTOPSY	TUBERCULOSIS AT AUTOPSY
		days				*days*	*weeks*	
I^{i}	Inguinal node		+++			15	8	+++
II^{i}	Emulsion					15	8	++
I^{ii}	Inguinal node	15	+++	Staphylococci			17	
II^{ii}	Emulsion	15				14	10	++
I^{iii}	Inguinal node	29	+++	?	+		16	
II^{iii}	Emulsion	29				10	4	+
I^{iv}	Inguinal node	43	+++	?			13	
II^{iv}	Emulsion	43				14	5	++

Moreover, the inert bacilli persisted and kept their normal morphology for a long time after planting in the new host. In one instance (I^{v}) a node, planted after thirty days' incubation and removed at autopsy after nine weeks in the new host, still showed many tubercle bacilli of normal appearance in the caseous areas, which had become partly calcified. The same was true, both as to bacilli and calcification, in another node planted after forty-three days' incubation and thirteen weeks in the host guinea pig ((I^{iv}). These pigs showed no signs of tuberculosis.

TABLE 2

GUINEA PIG NUMBER	GIVEN	TIME TISSUE OR EMULSION HAD BEEN IN INCUBATOR	RELATIVE NUMBER OF TUBERCLE BACILLI IN SECTIONS	CONTAMINATION OF TUBE	ABSCESS AFTER PLANT	TUBERCULOSIS OF HOST'S INGUINAL NODES FIRST NOTED	TIME ELAPSED BETWEEN PLANT OR INOCULATION AND AUTOPSY	TUBERCULOSIS AT AUTOPSY
		days				*days*	*weeks*	
I	Inguinal node	2	+++	Staphylococci	+	19	9	++
II	Liver	2	+	?	+	43	9	+++
III	Emulsion	2				19	12	++
I^{i}	Inguinal node	7	++				12	
II^{i}	Inguinal node	7	++	Staphylococci	+		12	
$\mathrm{III}^{\mathrm{i}}$	Inguinal node	7	+++				16	
IV^{i}	Emulsion	65				20	3	+
I^{ii}	Inguinal node	11	+++				12	
$\mathrm{I}^{\mathrm{iii}}$	Spleen	23	+++				13	
$\mathrm{II}^{\mathrm{iii}}$	Inguinal node	23	++++	Staphylococco			12	
I^{iv}	Inguinal node	21	+++				5	
$\mathrm{II}^{\mathrm{iv}}$	Liver	21	+				13	
$\mathrm{IV}^{\mathrm{iv}}$	Salt solution from liver tube	21					15	
I^{v}	Inguinal node	30	Whole node planted—no sections				9	
II^{v}	Inguinal node	30	Whole node planted—no sections	Staphylococci	+		14	
$\mathrm{III}^{\mathrm{v}}$	Liver	30	Whole tissue planted—no sections				14	
IV^{v}	Salt solution from liver tube	30					15	
V^{v}	Emulsion	87				13	8	++

As a rule the planted tissue was mostly absorbed in a short time, and autopsy showed only a small brown area, which on section consisted of large endothelial phagocytes containing fat and pigment. Sometimes tubercle bacilli were demonstrated in these cells (I^{iv}), which often coalesced to form giant cells of the foreign body type. The tissue reaction, that is to say, resembled that produced by any inert insoluble foreign material. The only changes noted in the regional nodes corresponded to those at the plant—slight to moderate infiltration with pigmented phagocytes. These phagocytes also carry some of the inert bacilli to the nodes, where we have sometimes detected them in small numbers.

We next did a third series to determine exactly when the loss of virulence occurs In this series we planted nodes after incubation periods of 1, 2, 3, 4, 5, 6, and 9 days. Those of 1, 2, and 4 days produced disease; the lesions in the four-day host were slight as compared with the one and two-day pigs, at autopsy after nine weeks, but this may have been a matter of dosage, since the node used on the fourth day was a very small one, while the others were large.

However, in this pig there was distinct early calcification in connection with caseation in the regional (right inguinal and iliac) nodes. Similar calcification was observed in the spleen of pig II, which was given tuberculous liver incubated two days, and by biting at the incision produced a primary infection of his peritoneal cavity. We have since observed calcification as a result of inoculation with a very few free virulent bacilli. The 3, 5, 6, and 9 day nodes had not produced any visible tuberculous lesions when autopsy was performed after eight to nine weeks (table 3A). From these experiments it appears that vascular connections between the host's tissues and the planted node must develop in the first few days after the node is planted, somewhat sooner, that is, than we believed when we published our first report.

Finally, we cut open and crushed two large caseous nodes before incubating them, thus setting many bacilli free on the surfaces of the tissue and in the salt solution, in order to find out whether we were right in believing that the loss of virulence was in some way a result of confinement of the bacilli in tissue. One of these became contaminated with organisms of putrefaction, and when planted after twenty-one days produced no tuberculosis. The other was not contaminated; it was planted after thirty-five days' incubation and produced manifest tuberculosis in the new host's inguinal nodes in twenty-one days (table 3B). No unbroken node incubated more than four days has caused tuberculosis in the new host in our experiments.

This prompt loss of virulence and apparent death of tubercle bacilli in tissue, without change in their appearance and staining, is at variance with many previous observations, which vary also among themselves. The following quotations illustrate the status of opinion on the subject:

TABLES 3 A AND B

GUINEA PIG NUMBER	GIVEN	TIME TISSUE OR EMULSION HAD BEEN IN INCUBATOR	RELATIVE NUMBER OF TUBERCLE BACILLI IN SECTIONS	CONTAMINATION OF TUBE	ABSCESS AFTER PLANT	TUBERCULOSIS OF HOST'S INGUINAL NODES FIRST NOTED	TIME ELAPSED BETWEEN PLANT OR INOCULATION AND AUTOPSY	TUBERCULOSIS AT AUTOPSY
				A				
		days				*days*	*weeks*	
I^{vi}	Whole small inguinal node	1	No sections			23	9	++
II^{vi}	Half of large inguinal node	2	No sections			22	9	++
III^{vi}	Whole medium-sized inguinal node	3	No sections				9	
IV^{vi}	Whole small inguinal node	4	No sections			31	9	+
V^{vi}	Whole medium inguinal node	5	No sections				8	
VI^{vi}	Whole large inguinal node	6	No sections	?	+		8	
VII^{vi}	Whole large inguinal node	9	No sections				8	
				B				
III^{iv}	Half of crushed large caseous inguinal node	21	++	Staphylococci and putrefactive bacteria	+		14	
V^{iv}	Salt solution from tube of node III^{iv}	21		Staphylococci and putrefactive bacteria	+		13	
I^{vii}	Half of crushed large caseous inguinal node	35	No sections			21	5	++

Baldwin (4) writes

> Putrefaction of sputum and tuberculous animal tissues usually destroys the tubercle bacilli within a few days (Baumgarten and Falk, de Toma, Schill and Fischer). It is dependent however on the nature of the process and how rapidly it takes place whether the products of decomposition are harmful to the bacillus or not. Galtier was able to infect animals after two months with putrid spleen and lung. . . . . Cadéac and Malet found buried tuberculous lungs virulent after five months, but Klein not after seven weeks.

Ravenel (5) cites the same authors and adds,

> Petri found that the tissues of a tuberculous rabbit remained virulent for three months and six days when buried in a zinc box, but for only one month and five days when a wooden box was used. Galtier found that tuberculous tissues immersed in water *renewed from time to time* remained virulent for two months.

Calmette (6) adds, "Schottelius says that the bacilli remain alive in phthisical cadavers for several years."

As a result of our experiments we draw the following conclusions, which may serve to reconcile divergent views:

1. Tubercle bacilli, enclosed in tuberculous tissue and kept in salt solution at body temperature, lose their virulence and probably die in a few days, regardless of whether contamination occurs or not.
2. Tubercle bacilli free in salt solution, or on the surfaces of crushed tissue, die in a short time when in close contact with certain types of putrefaction, but survive for a long time in the absence of putrefaction.

The most plausible explanation of these facts seems to be that the bacilli confined in slowly dying tissue, and the bacilli in intimate contact with putrefaction, which involves reduction, are deprived of oxygen, and soon die from this cause; while bacilli which receive the necessary minimum of oxygen survive for a long time. Such conditions of aeration may exist on the surfaces of putrefying tissues exposed to air, and even immersed in water "renewed from time to time," as in Galtier's experiment. However, we are not prepared to exclude some specific lethal effect of the tissue itself, as suggested by Manfredi and Frisco (7) and Bartel (8). In 1909 Fontes (9) reported experiments in which an extract of tuberculous guinea pig lymph nodes greatly reduced the number of carbol-fuchsin-staining tubercle bacilli in an emulsion, while an extract of normal nodes had no such effect. In his report he makes no mention of the effect on virulence, and we have not been able to find in the literature any expansion or confirmation of his work. Some such factor may operate in our experiments. Calmette, however, attributes Fontes's results to agglutination.

The fact that the bacilli die so quickly in excised tissues inclines one to believe that when tubercle bacilli survive and keep their virulence for a long time in supposedly healed lesions, they are not completely encapsulated, nor entirely isolated from the host's metabolism, but rather held in a state of minimum activity, a sort of hibernation in which there is still some biological exchange between them and the host's tissues. This view seems more consistent with the current theory that the existence of such lesions is accompanied by active immunity against a new infection. It also offers some encouragement to our hopes of finding some successful method of chemotherapy in tuberculosis. But this lies outside the limits of our present experiments.

This much we do know with approximate certainty: that tuberculous nodes upon removal from the original animal, and for a very few days thereafter, contain virulent bacilli capable of producing manifest lesions in a fresh host, usually in two to four weeks; but that after these nodes have been in normal salt solution in the incubator for a week or less the bacilli have completely lost all power to produce such lesions in a fresh host—at least, no tuberculous lesions appear in eight to twelve weeks after the tissues are planted.

This calls for a continuation of the experiments, to find out whether it is simply a matter of the bacilli being alive or dead, or whether there are stages of attenuation between, say, the second and seventh days, in which we may have bacilli which do not produce the usual disease, but may be capable of producing retarded or otherwise modified lesions. We shall have to inoculate another series with nodes 1, 2, 3 days old and so on, and keep these pigs alive for six months to a year, in order to see if any of them develop anything suggesting an attenuated infection.

If this proves to be the case, it will be desirable to attempt some immunizing experiments with incubated nodes, on the analogy of Pasteur's antirabic vaccination with dried infected spinal cords, beginning with the very attenuated and working up to the virulent. In the absence of any practical method of immunization against tuberculosis, all such ideas are extremely seductive, but must be tested in a very deliberate and critical spirit.

This research has been made possible through the generosity of Mrs. B. C. Allen of Colorado Springs.

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WHAT CONSTITUTES THE EARLY RECOGNITION OF TUBERCULOSIS?[1]

SELIG SIMON

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Krause (1) in an address on *The Nature of Resistance to Tuberculosis* aptly sums up the efforts of all tuberculosis workers when he says:

> The field is tremendous and has hardly been scratched in a systematic way. We must study the biology of these pathological formations in a developmental manner from the first signs of reaction to irritation right through to ultimate loss of tissue. For many years our pathologists have only too often sought to unravel our most difficult problems by meticulous observation of cavity and cheesy patch. But the slender threads that hold the solution to the riddle have long been cut down in the cavity.

To me there seems little doubt that the results obtained in the application of the tremendous study on tuberculosis have fallen far short of the effort. Our present knowledge or, better perhaps, the application of that knowledge, has not materially changed tuberculosis morbidity, though mortality has unquestionably been lowered through the medium of the sanatorium and other factors.

When I speak of morbidity, I refer to the number of individuals, known and unknown, who as a result of tuberculous disease are rendered unfit, partially or wholly, to pursue their occupations in the productive sense of normal healthy people. So, too, the factor of diagnostic error looms strong in mortality, but its constancy, formerly and now, makes a lessening death rate seem plausible and actual.

It is permissible perhaps to venture the thought that research tuberculosis and clinical tuberculosis are separated by a chasm of infinite depth and distance. The investigator and the clinician have everything in common but nothing in particular: the one strives to learn a means of cure; the other strives to cure without means.

In this brief paper an effort will be made to point out paths by which investigative knowledge may be brought closer to clinical practice.

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[1] Read before the Trudeau Society, St. Louis, April 7, 1921.

It is conceivable, and in large measure conceded, that in thickly populated communities, such as cities, every human being sooner or later comes in intimate and repeated contact throughout life with living virulent tubercle bacilli. It is further conceded that in "practically every instance the tubercle bacillus enters the body by way of the air passages or the digestive tract or both. To exert its characteristic effect—to produce tubercle—it must get through the epithelium and INTO the tissues of the body. In the vast majority of cases it takes the path of the lymphatic vessels" (2).

It seems perfectly logical to assume that inasmuch as the lymphatic system drains every part of the body there can be no infection of the body "without there being at some time or other infection of some part of the lymphatic system. . . . . We must remember too that lymphatics encircle and course along the entire respiratory tract even to the terminal bronchioles, the length of the alimentary canal, and the entire venous and arterial systems of the body" (2).

Miller (3) describes the lymphatic system and lymph flow in the human lung as follows: Grossly there is a superficial and a deep set of lymphatics, the former in the pleura, the latter accompanying the bronchi, pulmonary artery and its ramifications, and the pulmonary veins; it also forms a dense network in the connective tissue septa between the secondary lobules,. The two sets communicate with each other in the pleura and at the hilum of the lung. No lymphatics are present in the walls of the air spaces distal to the alveolar ducts. No lymphatics are present along the veins which arise from the walls of the alveolar sacs. Where the venous lymphatics join the pleural lymphatics valves are present, but throughout the lungs the lymphatics are, as a rule, destitute of valves. Valves are present in the pleural lymphatics but they are so arranged that they prevent the flow of lymph into the lymphatics of the lung. The pleural lymphatics drain into the hilum nodes. The pulmonary vein which takes its orgin from the pleura and passes into the interlobular septum is accompanied by a single lymphatic with a valve pointing toward the pleura, and it is this short and often obscure vessel which provides a by-path for the lymph when its free flow toward the hilum is prevented. It is important to remember that under normal conditions lymph drainage within the lung is toward the hilum. If drainage is prevented the flow is into the pleura by the by-path just mentioned. Valves permit the flow of lymph from the lung into the pleura and prevent the flow from the pleura into the lung. Miller has never seen lymphatics unconnected with lymph nodes leaving the lung, and we know that from the lymph nodes drainage is into the thoracic duct.

The clinical significance of these findings must be left for future discussion.

Cornet's inhalation experiments with bacilli of low virulence in dust caused, you will remember, definite tracheobronchial node tuberculosis, though none was found in the lung. Krause (4) has shown that when normal guinea pigs are inoculated with an avirulent strain of tubercle bacilli in small doses, manifest tracheobronchial tuberculosis results without any demonstrable evidence of tubercle in the lung.

This is in direct opposition to the teaching of Ghon (5) who insists that tracheobronchial node lesion in human beings arise from pulmonary lesion, because, first, whenever tubercle is found in the tracheobronchial node it is likewise found in lung, and second, changes in the lung are always older than those in the gland. In this connection Krause says:

> Ghon's method of determining the comparative ages of lesions is open to severe criticism, and almost every student who has been accustomed to observe the development of tuberculosis and its spread from point to point in animals of experiment would be inclined to quarrel with him. In two tissues that differ so much as that of lymphatic nodes and that of lungs, the occasion must not infrequently arise that would make it almost impossible that the development of tubercle in one would keep pace with the development of tubercle in the other, even though the numbers of infecting bacilli that were brought to particular points in each tissue might be the same—and this is highly improbable. Even in the same tissue tubercle does not proceed at the same rate; and if considerable time—years perhaps, as in the human being—has elapsed since infection it may be totally futile to attempt to determine the relative ages of lesions. In fact, in my animals that were described above, only a few months after infection, lymph nodes like the tracheobronchials that were remote from the portal of entry, sometimes showed changes that in every way appeared to be older than those that were tributary to the point of inoculation; yet we are absolutely certain that lesion and infection developed in the latter first.

The tracheobronchial nodes are the converging point for lymph that drains the lungs. Tubercle bacilli can get into these nodes ordinarily by way of the lymph from the lung and through the bronchial arteries, and the possibilities of their infection are overwhelmingly in favor of the lymph. Since the lungs are the converging point ultimately of all foreign particles that, gaining the lymph stream and passing through interspersed glands reach the venous system, so the tracheobronchial glands can become the converging point for all foreign particles that enter the body and reach the lymph and venous blood streams.

These observations do not preclude the possibility and the probability that anywhere and everywhere tubercle bacilli may be arrested in viscus or tissue and produce tubercle, but the number so arrested are few, the lesion they produce small, discrete, capable of successful attack and ultimate encystment with no harmful effect; while the far greater number continue their migration and are ultimately arrested in tracheobronchial nodes.

Viewed from this angle, it is easy to understand how lungs on X-ray plates and at autopsy show discrete healed tubercle without any evidence of clinical tuberculosis; and in the presence of clinically demonstrable tuberculosis these same lesions remote from and apparently unassociated with the process produce signs and symptoms.

The time at which these healed tubercles appear in the body depends largely if not wholly on the number of bacilli that gain entrance thereto in a particular individual, and the filtering out of such bacilli in small numbers from the lymph and blood streams as the masses are slowly borne to the lungs and eventually the hilum glands.

In the fulminant type of disease, Clough (6) and others have recovered tubercle bacilli by culture from the blood of such patients and I have demonstrated tubercle bacilli in the urinary sediment of patients suffering from chronic pulmonary tuberculosis with bacilli-laden sputum, who gave no symptoms and whose urine showed no evidence of kidney disease.

Now then, if the hilum glands do indeed carry the brunt of the burden of infectious material such as tubercle bacilli, we would expect as Krause has shown experimentally, that they would show early lesion, and further, that as a result of such early lesion, there would be an ever increasing sluggishness of the lymph flow; that bacilli would tend to accumulate in the lymphatics and tissues near the hilum, and that tubercle formation would be accelerated in this neighborhood; that extension would proceed from this area outward and toward that portion of the lung where movement was least and consequent sluggishness of lymph flow greatest—namely, the apex.

If this concept of spread of infection and lesion be true, then all superficial tuberculosis, that is, recognizable parenchymal involvement, is not early but advanced disease, with hope of cure remote. The recognition of early tuberculosis then would centre around the hilum, and if, in this area, that is, between the second and the fifth dorsal segments in the interscapular space, we elicited impaired resonance, harshened whisper and bronchial breathing or any modification of these different from the normal, we would be justified in assuming that here we had evidence of a beginning parenchymal tuberculosis which left unchecked would spread to the surface causing widespread disease. The physical findings noted above are comparable to those so frequently suggested by the pediatrist interested in tuberculosis, though he attributes his findings to tracheobronchial lesion, when in truth the process has already involved the deep lung in this neighborhood. Greenberg (7) in a paper on *Chronic Tuberculosis Hilus Pneumonia in Children* remarks that "the type of tuberculosis to which I wish to call attention may be defined as a diffuse or parenchymatous process involving that portion of the lungs immediately adjacent to the hilum." Further: "extensive tuberculous lesion about the hilum may occur in infants and young children which pursues a rather chronic course. Recovery probably takes place in the majority of these cases even in children under two years of age."

It might be possible to so infect guinea pigs as to show the process of damming back of lymph with progressive development of tuberculosis from the hilum outwards.

The autopsy table has brought home the knowledge that wherever lung tuberculosis is found there also is found involvement of the tracheobronchial nodes; that so called adult tuberculosis occurs in infants (8); that the cone and collateral circulation of Dunham (9) is an expression of the probable fact that what eventually proves to be clinically recognizable tuberculosis always begins at the hilum and diverges along the lymphatics as they, the lymphatics, converge toward the hilum. Postmortem statistics on children and infants always reveal more striking phenomena as regards tuberculosis than adults.

Wollstein and Spence cite the case of a three year old child with two cheesy tubercles in a bronchial lymph node at the hilum while the pia mater was the only other structure involved in the tuberculous process. In nine cases of intestinal tuberculosis they found two cases with lesions in the bronchial glands and none in the lungs. Most significant is this statement: "There were four children whose lungs contained recent miliary tubercles, while their bronchial nodes were free. Evidently the route of infection was through the blood stream." An infant nine weeks old, dying of meningitis showed a generalized tuberculosis in which "a cavity in the right upper lobe seemed to be the oldest lesion." In 184 necropsies on tuberculous children between six weeks and five years there was not a single case of healed tuberculosis.

Dunn and Cohen (10) found in 661 consecutive necropsies in children under two years old that 138 or 20 per cent showed tuberculous lesions. This suggests how frequently the disease is overlooked clinically.

In 3100 admissions to the Infants' Hospital, Boston, 291 had a diagnosis of tuberculosis confirmed. This hospital accepts patients up to two years of age.

I have been much interested in the question of infection and superinfection in tuberculosis. In the light of the above considerations it would seem that infection is not a fixed and static thing, but that it usually continues from its first assault in childhood throughout life; that if the dose of the first infection be sufficiently large and occur very early in life, we have fulminant disease or miliary tuberculosis; but if, as is more usual, the number of bacilli entering the body at any one time be small, reaction ensues in a regular and systematic but asymptomatic manner. This is not in conflict with the well known experimentally proved phenomenon that with the first infection there is produced a hypersensitive soil to all subsequent infections.

We may venture the thought, basing our line of reasoning on these premises, that if every civilized human being lived long enough, he would sooner or later show unmistakable evidence of clinically recognizable parenchymal tuberculosis. We might go further and say that in the large majority of people, throughout their lives, there is a reciprocal adaptation between host and bacillus, and that, when for one reason or another this adaptive mechanism breaks down, the parasite gains headway. In considering the tubercle bacillus in its relation to its host, we must look upon the "organism as the constant and the body as the variable."

Bacteriologists, working on the chemistry of the tubercle bacillus, have found structures of intricate complexity. Through its long symbiosis with body cells, it has acquired resistant structures that insure its safety and protect its life under most adverse circumstances. It has continued to live after being shut up in calcified tubercles for a quarter of a century; it has been rejuvenated from sputum twenty years old. Its ubiquity and the universality of animal infection compel us to think that its inherent structure is intimately bound up with and evolved from infinitely long parasitism in the animal body. It has grown and developed with human and animal life since life began and man will never be freed from its undesirable presence until he can so alter his body cells as to bring about this parasite's death.

SUMMARY AND DEDUCTION

Tuberculosis is a disease of repeated infections throughout an individual's life.

Tubercle bacilli, once they gain entry to the body, reach the lymphatic system. Relatively few are arrested in intercalated nodes or collections of lymphoid cells. The larger number are borne along through the venous system to the lungs where they are spread over the vast surface of pulmonary capillaries. Here too the smaller number may, as they leave the vessels to be again taken up by the pulmonary lymphatics, become arrested in collections of lymphoid cells or small lymph nodes but the larger proportion are borne with the lymph stream to the tracheobronchial nodes, where they set up definite lesion.

The only exception to the above is in the fulminant form of disease, and even here the same phenomenon may occur.

Tuberculosis near enough to the surface of the chest to be clinically recognizable is always advanced disease.

Early pulmonary tuberculosis, clinically recognizable, always begins at the hilum as an extension from the tracheobronchial glands, is deep seated, gives few signs in varying degree, consisting of impaired resonance, bronchial breath sounds and harshened whisper, between the 2nd and 5th dorsal vertebrae in the interscapular space. Tracheobronchial lesion without extension into the lung gives no physical signs.

The cure of tuberculosis is the eradication of the tubercle bacillus.

The arrest of extension of disease is appropriate treatment when the process is confined to the deep lung in the neighborhood of the hilum.

When the process reaches the surface all treatment is palliative.

The furthest advanced tuberculosis need not be incompatible with life and even with a fair amount of work.

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THE PROBLEM OF THE CHILD WITH LATENT TUBERCULOSIS[1]

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At a recent meeting of the Chicago Medical Society, a very interesting and instructive paper on latent tuberculosis in children was presented. The symptoms were described in an unobjectionable manner, and it was clearly indicated that, in the majority of cases, demonstrable lesions existed. Unfortunately, the essayist came to the conclusion that latent tuberculosis in children did not require any special treatment beyond attention to general hygenic and dietetic requirements. In the discussion this conclusion was concurred in.

In a very few remarks, made during that discussion, I took the liberty to record my objection to this view, pointing out that very much might, and should, be done for children with latent tuberculosis. I should like to enlarge upon this point, for further discussion.

Incidentally, the reporter of that meeting made me say that, in a study of something less than one thousand children, in Asheville, I found that tuberculous childen, whether active or latent, gained more rapidly in weight, absolutely, than normal children. Without explanation, that assertion is, of course, absurd. The remarkable gain was observed *after* these children had been actively immunized. Hence their rapid gain until they had reached the normal weight for their respective age periods.

It is not so many years ago that the existence of occult or latent tuberculosis in children was denied outright. It was asserted without qualification that in infants tuberculosis was invariably fatal, while in children, say, from two to six or eight years old, it caused early death in the majority of cases. When Behring first suggested it (1903) and formulated his famous dictum that adult phthisis is but the last stanza of a song the first stanza of which is sung to the infant in the cradle, the idea was received with anything but acclaim. The infantile and even the child's organism was held to be so definitely nonresistant to the pathogenic action of the tubercle bacillus that it was taken for granted that tubercle bacillus infection in infants and children gave rise to tuberculous disease unfailingly.

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[1] Read before the Chicago Academy of Medicine, January 27, 1921.

In the following years, more especially around 1910 (with the local tuberculin tests of Pirquet, Wolff-Eisner, Calmette, Moro and others), the assertion made by Behring was found to be based on fact; so that pediatrists and pathologists, like Schlossmann, Hamburger, Andvord of Christiania, and others, published many contributions on the subject of tuberculosis as a children's disease.

United States government statistics show that in the past four years nearly 1,500,000 children under ten years of age have died in this country. As long ago as 1912, the United States Bureau of Education warned us that there were in this nation 400,000 children with organic heart disease; 1,000,000 with tuberculosis; 1,000,000, with spinal curvature; 1,000,000 with defective hearing; 4,000,000 suffering from malnutrition; 6,000,000 with enlarged tonsils or other glandular diseases; 10,000,000 with defective teeth; and 15,000,000 who needed attention for physical defects prejudicial to health.

While it is understood that, many times, these figures count the same children for various ailments and there is, therefore, some duplication, the great fact remains that, in a population of roughly 110,000,000 there are 15,000,000 children, more than 10 per cent of the total population and a far greater proportion of the child population, physically defective. Since, in most instances, these defective children belong to that part of the population that is reached by dispensaries, to the lower middle classes and still lower strata of society, the problem becomes all the more grave if it is remembered that it is these portions of the population that procreate most energetically and produce the coming generations.

It would be foolish to claim that all the 15,000,000 defective children require treatment solely on account of latent, inactive or active tuberculosis. Still, I venture to say that especially latent and inactive tuberculosis, most frequently unrecognized, is responsible for the greatest part of existing physical deficiencies and that it could be eradicated by suitable treatment.

The warning contained in the figures cited is repeated strongly in some data contained in Monograph No. 5 of the Framingham Demonstration Publications (Medical Series III). It appears that, of a total of 460 children up to seven years old, 84 boys and 70 girls gave a positive reaction to the cutaneous tuberculin test. Yet, on physical examination of the reacting children no active cases of tuberculosis could be discovered, even in those children under five years of age. If we keep in mind that Framingham is an average American town with an average American population and corresponding morbidity rate, including that of tuberculosis, it becomes evident that at least a number of those 154 children reacting to the Pirquet test will ultimately acquire active tuberculosis, unless measures are inaugurated to eradicate the infection while it is in its latent stage.

Postmortem statistics and the results of tuberculin tests undertaken on large numbers of persons indicate that, of all adults, about 90 per cent carry a tubercle bacillus infection, a latent tuberculous focus, somewhere within their body. This focus causes clinical tuberculous disease in about 25 per cent and becomes fatal in about 9 per cent. Andvord, of Christiania, estimates that clinically manifest tuberculosis is probably from 10 to 20 times more frequent than are the fatal tuberculosis cases. It follows that clinical tuberculosis heals in the majority of cases and, also, that it must pass through a more or less prolonged latent stage which may last for years, even many years.

The tuberculin tests of the last decade have shown that the tuberculization of the population, that is to say, the general infection with the tubercle bacillus, is accomplished by about the fourteenth year of life. In most of these cases, the infection remains latent and may never cause any active or serious trouble. Although this is reassuring, it cannot be denied that the latent infection is potentially harmful, comparable to a lighted fuse near a powder magazine.

While the majority of those infected with the tubercle bacillus never experience any definite harm from this latent focus, there are certain individuals, especially those with a physical "predisposition" or with constitutionally receptive peculiarities making them liable to tuberculous disease, also those living under unfavorable hygienic and other environmental conditions, that will ultimately succumb to the disease unless active steps are taken to produce in them an active immunity against the injurious action of the tubercle bacillus.

The danger lurking in a latent tuberculous focus is indubitable, since Lydia Rabinowitsch, Julius Bartel and others have shown that calcified and other apparently completely extinct tuberculous foci might contain living and virulent tubercle bacilli which produced active tuberculosis in guinea pigs. Hence, it evidently is not sufficient that the tuberculous focus, even though it be latent, be entirely walled in by a fibrous capsule and eventually become calcified. It manifestly is necessary that, before their imprisonment in the fibrous capsule, the tubercle bacilli be subjected to the bactericidal and bacteriolytic action of the fully immune tissue fluids. If such an active immunity is not developed spontaneously, as occurs in the normally functioning human organism, it should be aided by means of active immunization.

Clinical tuberculosis develops in those infected children who do not respond to the bacillary invasion with a sufficient antibody formation. Whenever the latter—the immunizing response—is adequate, an infection will not develop into the corresponding infectious disease, no matter what may be its nature. Infectious disease is invariably a sign of a bankrupt immunizing apparatus.

The line between the latent, inactive tuberculous focus and the "masked juvenile tuberculosis" referred to by Cooke and Hempelmann (AMERICAN REVIEW OF TUBERCULOSIS, November, 1920, p. 660) is exceedingly fine. Any little disorder, a cold, an attack of one of the exanthems, strain, exposure, and so on, may cause the latent focus to pass into the active by way of the masked form.

Facts justify the assumption that the latent focus may persist for a few days or for many years. However, it is not said that, during a long duration of latency, a tuberculous focus is necessarily without more or less manifest influence upon organic well being and functioning. As it must be admitted that actual organic changes precede by variable extent and period the possibility of clinical recognition of tuberculosis, so it must be granted that between the dormant, latent, stage of tuberculosis and the active invasion into the tissues of the tubercle bacillus, there is included a period of more or less intense bacillary metabolism wherein bacillary products are thrown off and cellular reactions are invoked—a series of vital changes that, indeed, constitute the essential chemical processes of tuberculosis; and yet all these may escape definite apprehension by our faculties.

The reason for this is that the merely toxic effects of the tubercle bacillus, due to its endotoxins, its "aggressins," or whatever you may want to call them, are not necessarily connected with the typical, classical, anatomical form of tubercle, the characteristic lesion due to the action of the bacillus on the tissues. The toxic tuberculous lesions have been designated as paratuberculous, secondary-tuberculous, and so forth, and have found a lucid interpretation, for instance, by Poncet and others in their descriptions of "tuberculous inflammation without tubercle," "tuberculous rheumatism," and similar affections.

Indeed, latent tuberculosis may manifest itself in a great variety of ways of which we may mention only a few in passing. Some of them may be frankly tuberculous; most of them do not show clearly recognizable signs of pathological tubercle. There are scrofula, rickets, Poncet's inflammatory tuberculosis and tuberculous rheumatism, Freund's narrow upper throax, the so called phthisical habitus and other stigmata of "pretuberculosis" or of the tuberculous "predisposition:" also gingivitis, enlarged tonsils, nasal and pharyngeal catarrh and all that this implies, sinus infection, ear infection and many other things. I do not claim that all of these are invariably tuberculous in nature or causation. However, they are so in a sufficiently large number of cases to engage our attention urgently. Even if they are due to other bacteria, they tend to weaken the organism and lessen its resistance against the latent tuberculous focus, usually in the hilum glands.

Since it has been established that the defensive and autoimmunizing mechanism depends, at least in part, upon a normal functioning of the endocrine organs and since it has been found that, in early tuberculosis, the thyroid and the adrenal functions are insufficient, evidences of weakness in that direction should call our attention to a possibility of latent tuberculosis. In the December issue of *American Medicine*, Harrower discusses this point and concludes that, if the thyroadrenal system is depleted, oxidation is diminished and the defensive apparatus is less efficient. By deliberate endocrine medication the lack may be supplied.

I believe that I have said enough to show that the problem of the child with latent tuberculosis is a real one; one deserving of our best and most serious efforts. To pass it off with an airy declaration that such children are not in need of treatment beyond general hygienic and dietetic attention is futile. These children have a latent focus because, at one time, their immunizing response broke down. True, it became reëstablished and the infection became latent. *But*, the latency may change to activity. Do not forget that it is from the ranks of the children with latent tuberculosis that the consumptives of the future are recruited.

What are we going to do about it?

It is evident that the frequency of active tuberculosis in adolescents and adults is still altogether too high. One reason is that the most important factor in the causation of adult tuberculosis, that of childhood tuberculosis, has been generally recognized only recently. Even so, while the weight of tuberculosis prophylaxis has—quite properly—shifted from adults to children, efforts in this direction have been entirely inadequate to cope with the subject. Childhood prophylaxis is still too largely theoretical. Of those children who live and grow up in particularly unfavorable environments, only a small proportion can be reached and supervised. Even with daily visits of the district nurses, too many unfavorable factors persist actively to negate the splendid work done by these devoted women. The annual outing of two weeks or so is available to but a very small number of children compared with the masses in need of it; and, alas, the two weeks' vacation is all too brief to accomplish lasting good. Even the adoption of Grancher's plan, as it is practised in the famous *Oeuvre Grancher*, can eliminate but a limited number of "phthisis candidates" and restore them to full health. The many tuberculosis dispensaries do yeoman work. But they too are far from reaching all who should be reached, nor can they do their work as thoroughly as it should be done.

One reason why children with latent tuberculosis should receive active treatment is to be found in the very occurrence, or development, of the tuberculous focus.

As is generally considered, tuberculous infection takes place in most cases in fairly early childhood, at the latest the first or second years of school life. This infection will progress to disease, accordingly as the normal, or physiological, defensive apparatus fails to function or as it becomes successfully activated. In the latter event, the defensive cells (lymphocytes and others) which are attracted to the tubercle bacilli that have invaded the mucous membranes or the submucous layers are stimulated by "agressin-like" substances to the formation of bactericidal and bacteriolytic substances. If the formation of these immune substances is sufficient quantitatively and qualitatively, the infection remains limited as such. Disease does not occur; on the contrary, the defensive cells have experienced a course of "training" which enables them in case of renewed infection to respond to that quickly.

It is different when this physiologic defensive, or immunizing, response on the part of the organism is not inaugurated. In case of failing resistance, the tubercle bacilli are enabled to exert their irritating and pathogenic action upon the tissues in which they are localized. Tubercles form in the manner with which we are familiar in the pathological descriptions, especially since Virchow. If an immunizing response fails altogether, progressive tuberculous disease is the consequence.

In a great many cases, the resisting mechanism becomes sufficient, sooner or later after the formation of a definite tuberculous focus, to arrest its further progress. It becomes inactive and latent and sometimes ceases to give rise to any systemic disturbances. In most cases, however, there are decided stigmata, mostly physical, although they may manifest themselves mentally and even psychically. There is especially a tendency to anemia, to anorexia, to digestive disturbances with resulting autointoxication; then also the endocrine insufficiency. The great majority of these children afflicted with latent tuberculosis are physically and, sometimes, mentally below par in some respect. Furthermore, the tuberculous focus, latent though it may be, is like a keg of powder in an old shack containing much inflammable material. It may take but little to incite it to activity. An attack of one of the exanthems, an exposure to the inclemencies of the winter months, the strain and fear attendant upon study for examination, and many other things may activate a latent tuberculous focus.

Quite evidently, the self immunization has not been quite sufficient, even though it succeeded in arresting the tuberculous process. If it had been maximal in degree, infection never would have progressed to disease at all. Therefore, the organism is in need of the outside support to the end that the immunizing mechanism may be stimulated and increased quantitatively and qualitatively to a sufficient degree.

In dealing with these children with latent tuberculous foci, it must never be forgotten that the latently tuberculous children of to-day are the consumptive adults of to-morrow. It is always to be kept in mind that adult phthisis develops usually upon the basis of a tubercle bacillus infection suffered during childhood.

For all these reasons, the need is quite self evident that all those children in whom a tuberculous focus can be discovered, no matter whether it be active, inactive or latent, should receive active and definite treatment through which their immunizing mechanism is trained in such a manner that it can produce a sufficient amount of immune substance on call, whenever that may occur, to overcome an existing infection and to neutralize any toxic substances (mostly endotoxins) that may develop. The feasibility of such a program has been demonstrated by practical experience in various places.

Most authors, in discussing general hygienic, dietetic and climatic means for raising or maintaining resistance, speak of theoretical, ideal conditions. They outline what *should* be done—how children should be protected from massive exogenic reinfection,[2] how they should be fed, housed, cared for, including removal to favorable climates. For instance Walter B. Metcalf (*Tuberculosis of the Lymphatic System*, New York, 1919, pp. 147–153) discusses the problem interestingly, and excellently—from the theoretical viewpoint. Still, his discussion merits earnest and careful study and observation.

Unfortunately, practice and reality, that is, actual circumstances, stand here as elsewhere in sharp contrast to theory. The majority of children who are most in need of protection against active disease, who most require highly favorable conditions of living, are members of families with decidedly restricted means. Ideal diet, housing, open air conditions, etc., are impossible. There is then only recourse to do the best one can.

Mary E. Lapham (*New York Medical Journal*, 1915, vol. ci, p. 108, and elsewhere) insists on periodical examination of school children, by which the first signs of active disease could be discovered. This was proposed years ago by Grancher to whose efforts the French prophylactic measures against tuberculosis are due.

Pottenger's discussion (*Clinical Tuberculosis*, St. Louis, 1917, ii, 503 seq.) also merits attention. Especially should his warning against the indiscriminate removal of tonsils in children (p. 506) be heeded. The danger of leaving latent or inactive tuberculosis infection unchecked is pointed out in volume i, p. 109, seq. (*ibid.*).

Pottenger wants to discover results of infection early, before physical signs have made their appearance, by means of tuberculin tests (vol. i, 110).

Therapeutically, in addition to general hygienic, dietetic, climatic measures, he says that much can be accomplished with tuberculin preparations.

> A prolonged course of tuberculin given children of this type during the age period from five to ten or twelve years will often be a determining factor in their development. Even after the lung is involved, they yield quite readily to proper treatment. The child has the advantage over the adult in

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[2] In case of children with latent tuberculosis, it is not so much the exposure to infection from open cases, as rather reinfection from their own foci, that may give rise to active disease. Therefore, everything should be done to extinguish that latent infection.

that it is in the period of growth and development. This is the period when the body cells should be at their best, because they have not yet been injured by excesses of various kinds and by various poisons which have been either taken into the body or elaborated within the body itself; consequently, this is a very advantageous time for the treatment of tuberculosis. If more attention were given the disease at this time, there would be a marked diminution in active tuberculosis during adult life; and, probably, no other factor would have a greater bearing upon the final solution of the tuberculosis problem.

Bandelier and Roepke (*Die Klinik der Tuberkulose*, 2 ed., Würzburg, 1912, p. 613, seq.) discuss the problem at length in its general aspects, insisting especially upon the importance of proper infant feeding and, then, of school hygiene. They advocate, in addition, exercises, care of teeth, since many disturbances of childhood (anemia, digestive troubles) that predispose to tuberculosis are sequels of dental disease. The tendency to insufficient thorax development (Freund) is to be combated by suitable exercise, so as to counteract a "phthisical habitus." They limit individual therapeutic measures to those with tuberculosis of endothoracal glands and the earliest forms of pulmonary tuberculosis.

Fishberg (*Pulmonary Tuberculosis*, 2 ed., Philadelphia, 1919, p. 543) mentions that, after endemic diseases, the body is in a state of anergy and requires special care with a view to preventing metastatic autoinfection.

This may be done by either taking the child to the country, preferably to the seashore, for a few weeks or months until it has completely recuperated; or, when it must be kept at home, it should be given proper nourishment and kept outdoors the greater part of the day, and it should sleep in a room with open windows.

All this is splendid where it is feasible. However, in the majority of cases, it is not. These children should be given individual care in dispensaries, when means preclude continued visits to physicians. Suitable tonics, including cod-liver oil, are of actual benefit. Catarrhal conditions of mucous membranes can and must be treated. The specific resistance must be raised to highest point.

In dealing with children with latent tuberculosis, we may remember that formerly these were considered as "specially predisposed" to phthisis and that is just what they are. Calmette-Petit (Petit, *Le diagnostic de la tuberculose par l'ophthalmo-réaction*, 1907, Paris) declared properly that "*les prédisposes sont des tuberculeux et non des tuberculisa-*

bles." It should always be kept in mind that childhood infection results in antitubercle-bacillus protection *only* if a complete immunity is produced. A latent tuberculous focus indicates a more or less temporary breakdown of this immunity. Therefore, active steps must be taken to prevent other breakdowns.

In his book, *Tuberculin and Vaccine,* Ellis Bonime devotes a brief chapter to the question of general prophylaxis. He insists particularly upon the elimination of pathological processes which so frequently occur in obscure recesses and occupy such small areas that they escape the notice of the patient as well as of the physician. Attention should be paid to the nose and throat, while periodic dental examinations should be had to remove conditions that are most frequently sources of mixed infection.

Regarding the consideration of dietetic measures, not only from the standpoint of nutrition but, what is more important, from the standpoint of assimilation, Bonime properly says that it should be our object to push the nourishment to the maximum point of tolerance, but absolutely limited by the amount of assimilating power of the individual. As soon as we exceed the power of assimilation by any quantity of food, we throw an added burden upon the already overtaxed system by forcing it to dispose of the surplus. And, since the circulation must be drawn upon in order to dispose of any surplus food, the circulation is diverted in an undue degree to the gastrointestinal canal, and an anemia is created at the point of infection. Improper feeding will thus interfere with or wholly prevent, one of the main assets in the conquest of disease—hyperemia.

Wolff-Eisner, Calmette, Petit and many others demand the deliberate searching out of children with tuberculous foci, not only by physical exmination but also by means of specific-reaction tests, and to subject those *reacting* to prophylactic care.

Of course, it would be futile to assert that, under certain environmental circumstsnces, all infected children necessarily develop active tuberculosis. Such a foolish assertion is well controverted by Raymond Pearl (AMERICAN REVIEW OF TUBERCULOSIS, 1920, iv, 688). A family consisting of a father with open tuberculosis and nine children, all living at home for years, under the same circumstances, all became unavoidably infected. Of the nine children, only two acquired active tuberculosis. Pearl properly sees a possible explanation in the influence of the constitutional factor in the etiology of active disease.

If the "latent" focus is entirely extinct, if there are absolutely no signs of physical deficiency, the child growing and progressing normally, active treatment is not necessary. Thus far, I agree with the generally prevailing opinion. However, in the majority of cases, the focus, which either was latent from the beginning or became so through successful self immunization, has given rise to certain physical stigmata, signs of physical deficiency. In such cases, care and attention are needed to restore normal conditions, or to establish them.

I had intended here to outline other procedures that have been suggested by many authors. All of them deal principally with the general, hygienic, dietetic and environmental improvement of the children's condition. One of the most notable of the actual undertakings in which some of these suggestions are being carried out is the *Oeuvre Grancher* with which you may be familiar. The late Professor Grancher proceeded on the idea that removal from danger eliminates it. In the work carried out under his name, the children of tuberculized families are placed in the country in healthy farmers' families and, whenever possible, are adopted. The results of this work have been very excellent. It would lead me entirely too far, however, to enter in greater detail into other suggestions.

With regard to the advice that is given so often, and obeyed with such pitiful faith (as though it were actually possible to carry it out), namely, to protect children against contact infection, I should like to say that the best way to fight a universal bacterial danger is not to run away from it, even if it were possible to do so; but, rather, it is to acquire the necessary specific protection against it through which the bacterial infection can be limited and rendered harmless. In this manner the struggle against smallpox was won, and its application to the prophylaxis against typhoid fever and diphtheria has recently been undertaken, and carried out, with full justice and success. In the same manner, only, can we hope to be definitely and lastingly successful in the struggle against tuberculosis.

The successful eradication of tuberculosis would be of even greater bearing than was that against smallpox. However terrible was that plague, its mortality was only about ten per cent of the total deaths while that of tuberculosis was, until quite recently, notably higher. The economic loss due to smallpox, however, was far less than that from tuberculosis, as it did not entail so protracted periods of illness and nonproduction. Severe epidemics, such as those of smallpox, slew their thousands quickly, and people became alarmed and demanded that the Government should do something about it. Tuberculosis is slow, insidious; yet, it slays its millions. Nevertheless, the people fold their hands and bow to the Will of God, which is their own inertia, their own unwillingness to bestir themselves.

The treatment to which those children under consideration are to be subjected is of various kinds. It goes without saying that general hygienic, dietetic and climatic precautions should be taken, the children being supervised with regard to their personal habits, to their domestic circumstances and surroundings, with respect to their food, their attendance in school, and so on. Since most of these children will show a degree of anemia which may be slight, it will be well to administer tonics that have a beneficial influence upon the content of hemoglobin and also upon the number of red blood cells. Iron and arsenic, also manganese, probably are the best drugs to be used for that purpose. In addition, nuclein preparations are of use, which may be given in such a manner, internally or by hypodermic injection, as to stimulate directly the defensive cell action.

In addition to a suitable and sufficient diet, it is often well to supply an excess of fats, the best form being cod liver oil. This, though, is objectionable in many cases because of its unpleasant odor and taste, and it may suitably be replaced many times by olive oil or corn oil. The iodine that is contained in the cod liver oil may well be supplied separately. Especially in children whose lymph nodes show a tendency to swelling, I have frequently seen very satisfactory results from the administration, say, for one or two months at a time, of syrup of iodide of iron, from 10 to 30 drops well diluted, three times daily, after meals.

In my opinion, which has been formed through observation of the activities of the von Ruck Research Laboratory for Tuberculosis, in Asheville, North Carolina, and elsewhere, as also through a careful study of the literature in point, I am convinced that for all children who have been infected with tubercle bacilli, immaterial whether the infection was followed by an actual tuberculous focus that was latent, inactive or active, specific immunization is required. In the active cases, it may be said at the outset, this specific immunization naturally is not prophylactic but rather therapeutic, and it must be undertaken with all the precautions that experience and observation have dictated for the administration of tubercle bacillus products, or tuberculin preparations, of any kind. We need not concern ourselves with this phase of the problem at all, since we are interested, more particularly, in the child with latent or inactive tuberculosis.

In these children, it is an important problem to increase the specific immunizing response in addition to the physician's efforts to raise their physical condition to as high a state of perfection as possible. The children may be immunized prophylactically so as to protect them against the later acquirement of active tuberculous disease. By active specific immunization, a "training" of the defensive tissue cells is accomplished, as was described graphically by Petruschky in his *Grundriss.* If this training is pushed to a little above the actual requirements, it will be all the more likely to result in renewed activity on the part of the defensive cells at those periods when either new exogenic infection takes place or when, for some reason or other, an endogenic reinfection is experienced. Petruschky has shown that, while the immunizing activity may cease, the ability of its reactivation is dormant and it becomes aroused whenever need arises, providing physiological conditions are favorable for it; in other words, providing that the strength of the organism is adequate.

It has been found that old tuberculin is not the best agent for prophylactic immunization against the activity of the tubercle bacillus. Old tuberculin, as is well known, contains more particularly the water-soluble constituents of the tubercle bacillus. There are, however, other products in this germ that are far more potent and potentially harmful, and against which a specific immunity is urgently needed. In addition to these, the pathogenic power of the tubercle bacillus fats is great. Much and Deycke have shown, and von Ruck has confirmed it, that it is possible to stimulate that formation of specific antibodies against these fat consitutents, for which reason this part of the immunization should be attended to in order to make the treatment complete. When, therefore, we select a preparation suitable for a complete and effective specific prophylactic immunization against tuberculosis, we naturally cast about for a preparation that contains all reactive corpuscular substances of the tubercle bacillus. As far as I know, there are three preparations in existence that comply with these desiderata. They are Much's "partial antigens," von Ruck's vaccine against tuberculosis, and Crofton's (of Dublin) "antigen." These three preparations are capable of stimulating a complete immunizing response to the action of the tubercle bacillus. Complement fixation tests have shown, by using the partial proteins as antigens, that "partial" antibodies are formed in response to their introduction: that is to say, specific antibodies to the specific tubercle bacillus proteins.[3]

It stands to reason that the more complete an immunity exists to the possible pathogenic action of the tubercle bacillus in an organism, the more fully this organism is protected against disease, even in the event of weakening influences, such as other infectious diseases, strains, undue efforts and exposures.

It would be easy to adduce parallels in support of my position. I need refer only to the vaccination against smallpox, and to the toxin-antitoxin immunization against diphtheria, both of which have received the approval and support of the best informed and most experienced observers in the medical profession. In the case of an infectious disease that is as prevalent as tuberculosis, a disease that takes so treacherous a course, being acquired in its seeds in early childhood and remaining quiescent, hidden, obscure, for years before it breaks out in almost unrestrainable force, surely there can be no reasonable opposition to the necessity of utilizing every means by which the deleterious action of the infection upon the organism can be obviated, by which health and life can be preserved. I am convinced that a deliberate and extensive immunization against the tubercle bacillus, especially among school children, would go far toward reducing the tuberculosis morbidity among adolescents and adults in ten, twenty and thirty years from now. In my opinion, the prophylactic immunization provides one of the most effective means for a successful antituberculosis campaign.

Dr. W. W. Crofton, of Dublin, declares that there is only one method of bringing up a low resistance to normal or of increasing a normal resistance, and that is by the production of specific antibodies in the individual, by inoculating him with a vaccine of the related microbe. In the case of a universal infection like tuberculosis, he asserts, it is the only measure that will protect when the constitutional resistance is lowered by the various environmental and inherited causes of low resistance.

In an interesting communication (*British Medical Journal*, 1915, i, 629), he relates that it has been his practice, for the last eight years, to urge the members of families whose parents were tuberculous or in which cases of tuberculosis had occurred, to undergo short courses of treatment with tuberculin. Under the use of T. R. for prophylactic purposes, the improvement in health in many of the members of tuberculous families has been most satisfactory and, so far, no case of tuberculosis has occurred among those so treated; but, as the author points out, the numbers are far too small to have as yet any value.

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[3] It may be added that Ferrán has based upon his peculiar views as to the nature of the tubercle bacillus a very logical and attractive method of prophylactic immunization. Particulars may be found mostly in the Spanish medical literature of the last few years. (See the *Quarterly Cumulative Index to Current Medical Literature*. Chicago, American Medical Association, 1918 and elsewhere.)

In two more recent publications, namely, *Pulmonary Tuberculosis, its Diagnosis, Prevention, and Treatment*, London, 1917, and *Therapeutic Immunization, Theory and Practice*, London, 1918, Crofton enters into the subject in greater detail and also gives particulars concerning his own tubercle bacillus "antigen" which he employs for the immunization of children and adults.

As some of you will remember, Karl von Ruck proposed a more or less general specific protection against the acquirement of tuberculous disease, in a paper presented before the Chicago Medical Society, in May, 1912. At that time he announced his vaccine which is a complete antigen, containing all the reactive constituents of the tubercle bacillus.

Although von Ruck was the first to place the specific immunization against tuberculosis upon a definite scientific basis, the method itself had been suggested years ago by various authors. So, Heubner, von Behring, Calmette and others had declared it as desirable. Petruschky had insisted for years upon the importance of prophylactic immunization, especially of children living in families in which there are tuberculous members, and he attempted to secure it by means of persistent periodic courses of treatment with tuberculin. In order to avoid the many disadvantages of subcutaneous injections, he finally developed C. Spengler's method of percutaneous administration, for which he later employed a liniment containing a glycerin extract of dried human and bovine tubercle bacilli, a small amount of which was applied on alternating places of the body at intervals of three days. The applications were made by the persons to be immunized, on their own bodies.

In Hela, a peninsula projecting into Danzig Bay on the Baltic Sea, which is inhabited by fishermen and is virtually isolated from the world, Petruschky instituted, in 1911, the deliberate "assanation" of all families in which there were tuberculous persons, or individuals who reacted to the tuberculin test. In addition to the very encouraging therapeutic results which followed, he succeeded in restoring the "pre-tuberculous" persons, mostly children with latent tuberculosis, to health and could report, eventually, that the inhabitants of Hela were entirely free from tuberculosis (*Beiträge zur Klinik der Tuberkulose*, 1914, xxx, 217. *Münchener Medizinische Wochenschrift*, 1915, lxii, 145).

If this can be accomplished in a small, circumscribed community, it is possible elsewhere, even in the face of greater difficulties; the problem being merely one of greater scope. In my opinion, the lesson taught us by Edward Jenner, almost one hundred and twenty-five years go, has not yet been fully taken to heart; nor is it being acted upon to its full extent. The struggle against all infectious diseases, more especially against tuberculosis, and particularly against latent tuberculosis, never can become successful by resorting to makeshifts. It can succeed only by heeding the lessons impressed by Nature herself, in the manner in which she overcomes infection spontaneously, in those vigorous enough to activate and mobilize all resources that are required for the purpose.

VACCINES IN THE TREATMENT OF TUBERCULOSIS[1]

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The treatment of disease by the use of vaccines has received much attention from the members of the medical profession for the past few years. Nearly every new idea, theory, or practice that attracts public attention has to pass through three stages. First, it is enthusiastically and often unintelligently praised; then comes a reaction and it is just as enthusiastically and just as unintelligently condemned. After this, we have sober examination and judgment, a lessening of extravagant claims and of equally extravagant condemnation; and we settle down to a more moderate but far more truthful estimate of our theory.

Vaccine therapy has been no exception to the general rule, and it has had to face these three stages of public opinion. It has already passed the first stage, probably the second, and, in some quarters at least, it has reached the moderate, conservative, third stage.

Probably no line of treatment has been so overdone as vaccine therapy. We may look in any pharmaceutical catalogue and find a very large part of the book devoted to shot-gun mixtures of stock vaccines for nearly all known diseases. It is reasonable to believe that in a few cases there is an element of error. Stock vaccines have the same action that any foreign protein has. In these cases we should use the known quantity, such as egg albumen or, say, only one organism of the vaccine such as typhoid, rather than the unknown or shot-gun stock vaccine.

Since 1905 vaccines have been used, with varying results, in the treatment of tuberculosis. Professor Wright (1) wrote convincingly on the subject at that time. Wescott (2) also reported very good results. Hirschfelder (3) reports favorable results from soluble vaccines of the pneumococcus and streptococcus. Bonney (4) restricts the use of vaccines "to patients who fail to show satisfying improvement under conservative management" and gives febrile cases as the best indication. Smith (5) says that in his series of cases autogenous vaccines caused decided improvement in temperature, pulse, expectoration and weight.

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[1] Read before the Denver Sanatorium Association, March 22, 1921.

Before going into the details of the vaccine treatment of tuberculosis, I would emphasize that there is a certain class of cases that are not suitable for this treatment.

In the first place, we must accept as a premise that we do not have mixed infection without a primary focus. This being true, it is obviously hopeless to try to treat such a patient with vaccines when what he needs is, perhaps, the extraction of a tooth. I will cite a case in point:

C. D., age thirty-seven, had been in a sanatorium eleven months. He had pulmonary tuberculosis, stage III, and was an ideal patient. He had a diffusely distributed mixed infection with râles almost all over both lungs. His condition remained stationary during his entire stay at the sanatorium. When he came under my care I advised an X-ray of his teeth. At intervals of from two weeks to a month I had one tooth extracted (notice that I say only one at a time) until six were removed. He had a slight hemorrhage during this time, but three months after the last tooth was out he began slowly to gain, and at the end of six months there is a marked improvement of every symptom. Without the extraction of the teeth nothing would have helped this man, but after their removal vaccine treatment was indicated.

After having dealt with such obvious offenders as teeth, tonsils, appendix, tuberculous bowel, infected sinuses, infected gall bladder, goitre, or what not, we may feel that the case is suitable for vaccine treatment, if examination reveals a fair to considerable amount of moisture in one or both lungs. It must be remembered that there are types of tuberculosis which grow steadily worse, and nothing will stop these cases from going on to their fatal termination. However, I have included this type of case in my analysis further on, lest my results of the vaccine treatment appear too optimistic.

REASONS FOR POOR RESULTS IN THE PAST

I think that the bad results in the past may be attributed to several causes.

In the first place, the idea of giving anything but autogenous vaccines is irrational, and results are impossible with stock vaccines in a disease like tuberculosis. Weaver (6) in studying the action of the streptococcus says:

Streptococcus vaccines should always be autogenous. The importance of this is more apparent as the study of streptococci by more refined methods has shown that there are many strains of streptococci which differ among themselves in essential immunologic peculiarities. A vaccine prepared from one strain might be worthless against an infection by another one. There is nothing to say in favor of a polyvalent streptococcus vaccine, supposed to be active against all types of streptococci. In multiplying the strains, the quantity of each becomes so reduced that the essential one, if present, is in such small amount as to be without therapeutic effect.

Streptococcus vaccines are contraindicated in acute and general infections. In these circumstances the body is already exerting all its powers to produce antibodies to counteract the infection. The addition of still more bacterial toxin results only in harm. In streptococcus septicemias, vaccines are useless. In subacute and chronic local streptococcus infections, autogenous vaccines, given subcutaneously, sometimes act very favorably. This is especially true of infections of mucous surfaces unassociated with accumulations in poorly draining cavities. The initial quantity should be small, from 10 to 20 millions, and in subsequent injections the amount should be gradually increased. Moderate local reaction is desirable, but general symptoms usually indicate that the dose given has been too large. The reaction from one injection should subside completely before another is given.

Secondly, the dosage in the past has been too large. We must begin with small doses and increase very gradually. It has been my practice to start with as low as five to ten millions.

Third, we must avoid reactions. This can be done by increasing the dosage slowly. Bruce says:

> To obtain the best results the dose of vaccine must not produce a constitutional reaction. When a constitutional reaction is produced there is a loss of body weight. The dose should therefore be too small rather than too large.

In the fourth place, the interval must be long enough. I give the injections at five to seven day intervals, using the longer interval as the dosage becomes larger. Bruce (7) gives his injections at fortnightly intervals.

Lastly, there is no use giving a moribund patient a course of vaccine. It is necessary for the patient to have some powers of resistance left before he can be expected to react with any antibodies. Hence, in acute infections and where there is considerable fever we have a positive contraindication to the use of vaccines. The fact of the matter is that in these cases vaccines would be like pouring oil on the flames.

PERSONAL OBSERVATIONS

I have made a study of 48 dispensary and 15 private cases, or a total of 63, in the past two years. Of these, 42 were males and 21 were females. The vaccines were all autogenous and prepared in the usual way. Only one organism to a vaccine was preferred but in a few cases two were used. We now never use more than one.

The organisms used were the streptococcus, Streptococcus hemolyticus, Streptococcus viridans, pneumococcus, pneumostreptococcus, and the pneumococcus and streptococcus together. The vaccine was usually prepared with five hundred million killed organisms to the cubic centimetre.

The summary of the vaccines and organisms present is as follows: A total of 77 vaccine courses was given to 63 patients. Autogenous vaccines were prepared from the streptococcus in 28 instances. These were given to 22 patients, of whom 2 took 3 courses, 2 took 2 courses, and the rest 1 each.

The Streptococcus hemolyticus was present in 29 vaccines and given to 22 patients. In one patient the course was given 3 times, in 5 twice and in the remainder once each.

The Streptococcus viridans was present in 3 cases and only one course given to each.

A pneumococcus vaccine was given in 8 cases, only one course being given to each patient.

In 7 cases a pneumostreptococcus was given, only one course being given to each patient.

A vaccine containing the two organisms, pneumococcus and streptococcus, was given to 7 patients.

Of the 63 cases 42 were diagnosed as pulmonary tuberculosis, stage III, 12 as stage II, and 9 as stage I. As a result this should be a fairly good test of vaccine therapy, for most of them, or 66 per cent, were stage III cases.

Tubercle bacilli were present in 41 of the cases and absent in 22.

RESULTS

In 24 cases there was a decrease in the amount of sputum, in 6 there was no change, and in 16 the sputum increased in quantity. In the remaining cases the records are not complete.

Nineteen cases are working. This does not mean that they all should work, but it may be wilfully, due to financial stress, or because we have permitted them to work.

Twenty-two gained weight. The maximum gain was 32 pounds. In this case the tubercle bacillus disappeared from the sputum.

Twenty became worse, 8 remained stationary, and 32 were considered improved both as to subjective symptoms and physical examination.

Three died: one of influenza, and two of pulmonary tuberculosis. These figures may not be complete, as it is very difficult to keep in touch with dispensary cases and some deaths may not come to our knowledge.

Of the 32 who improved, 15 were in stage III, 10 were in stage II and 8 were in stage I. Of the remaining 31 who remained stationary, got worse or died, 27 were in stage III, 2 were in stage II and I was in stage I.

BENEFITS OF DIFFERENT ORGANISMS

Of the 7 cases treated with the pneumostreptococcus, 3 improved and 4 became worse or remained stationary.

Of the cases treated with pneumococcus vaccines, 3 improved and 5 remained stationary or became worse.

Of the cases treated by the streptococcus vaccine, 11 improved and 11 remained stationary or became worse.

Of those treated by the streptococcus viridans, 2 improved and 1 remained stationary.

Of the 22 cases treated by the streptococcus hemolyticus, 15 or 68 per cent improved and 7 remained stationary or became worse.

DISCUSSION

It will be observed, of course, that the most satisfactory results were obtained in stages I and II. However, improvement in 15 cases out of a total of 42, or 35 per cent of all the stage III cases, is significant. In the whole series in all stages there was improvement in 33 of the 63 cases or 52 per cent.

The results with the different vaccines are interesting.

The most distressing outcome was noted in a case treated with a vaccine containing both the pneumococcus and streptococcus. I will cite his history in more detail:

G. T., male, age twenty-seven, musician, native of Indiana; his father and mother are living but neither is strong. One brother has active tuberculosis.

The patient had influenza and pneumonia in November, 1918, from which he did not completely recover. In March, 1919, he expectorated about 3 ounces of blood. Since then he has had a persistent cough. In the same month tubercle bacilli were found in his sputum. He came to Denver on March 23, 1920, but could not be induced to go to a sanatorium. On April 5, 1920, he came to the dispensary. At that time he weighed 163 pounds. We then classed him as stage II. He was expectorating 2 ounces of yellowish-white sputum in twenty-four hours. His pulse was always high, 108 to 120. At this time there was no fever. July 16, 1920, his weight was 154 pounds. We then started a vaccine containing 500 million streptococci and 500 million pneumococci to the cubic centimetre. At the same time he was also given a course of sodium cacodylate. July 8th, one tonsil was removed under local anesthesia by Dr. T. E. Beyer. The patient's tonsils were so bad that it seemed advisable to get rid of at least one. He gradually became so much worse that he returned home having lost 8 pounds. He was worse in every way, sputum increased in quantity, and was running some fever.

Of course, this man was running down before he came to us, but it always impressed me that the vaccine should not have been given with both organisms present.

A few of the patients made most remarkable improvement. One dispensary case made an especially good record:

E. S., age forty-one, rubber tire manufacturer; father died of pneumonia mother is seventy-three, living and well. One brother died of tuberculosis, one sister living and well. Patient has never had any serious illness. In 1914 he began to cough and had some pain in the right side of the chest. His physician advised him to come to Colorado, and he arrived in Denver shortly after. His sputum in 1914 was positive. He felt he had to work, so he worked in the rubber tire business until September, 1919, when he was forced to stop. He came to the dispensary November 18, 1919. At this time he weighed 136 pounds, the sputum was positive for tubercle bacilli, and he was considered a stage III case, having râles after cough over the whole right side and the apex of the left front and back. We tried rest and the usual regulations first, but he remained stationary. May, 1920, a course of autogenous vaccine was started. The organism was the streptococcus hemolyticus, 1 cc. containing 500 million killed organisms. During the course of the vaccine the sputum was reduced from 4 ounces at the beginning to one-half ounce at the end. Its character changed from yellow to white. Beginning November 26, 1920, his sputum has been continuously negative for tubercle bacilli and has remained so. He has gained 32 pounds and is working. Posteriorly at both extreme apices after cough there is still a little moisture.

EXPLANATION OF RESULTS

It is difficult to explain the satisfactory results obtained in the above cases, but Bruce's (7) reasoning seems to me the most logical. He explains the action of vaccines on the body by the fact that nature produces a specific bacteriolysin, and, if toxins are also included in the injection, a specific antitoxin. There is also a specific substance produced which enables the leucocytes to ingest the bacteria. This substance was designated by Wright as *opsonin*.

In addition to all these there is a further action, which is not specific in character and which is always associated with an increase in the polymorphonuclear leucocytes. This action consists in a raising of the general resistive power of the body to any bacterial infection. Bruce adds:

> When my colleague, Dr. C. J. Shaw and I, were working at opsonic indices, we found that in healthy persons it was possible to raise or depress the index to the tubercle bacillus by injecting staphylococcus vaccine. A small dose of staphylococcus raised the tuberculous index and a large dose lowered it. The same results were obtained when testing the streptococcal indices of maniacal patients.

The fact which most impressed me was that the injections of the vaccine apparently stimulated nutrition, as 8 out of 11 cases markedly increased in weight. The weight began to increase after the first injection and continued to increase for a considerable time after the doses of the vaccine had been discontinued; after the stimulating affect had passed off weight was again lost.

To explain the stimulation of nutrition, therefore, it is necessary to look for some action more general than specific action. According to Ehrlich's theory of cell nutrition, there exists in the protoplasm of an active cell a nucleus with which the special functions of the cell are associated. This nucleus has attached to it a number of atomic groups or side chains, which play an important part in the work performed by the cell. These side chains readily enter into combination with suitable group atoms presented to them, and it is in this way that the nutrition of the cell is maintained. When toxin molecules are introduced they also can enter into combination with the side chains and for the time being exhaust the supply. As side chains are, however, in some way necessary for the life of the cell, the cell is stimulated to further production until finally the side chains are produced in excess. And if present in excess they will combine with other suitable group atoms.

This theory, I believe, explains the improvement in nutrition which in some cases follows the use of vaccines. We may take it that, in malnutrition which is persistent, the cells are of themselves unable to produce a supply of side chains to carry on healthy nutrition. When toxin molecules in the form of vaccines are introduced in suitable quantities the cells are stimulated to produce an excess of side chains.

It seems to me further, that the vaccine must be the most effective weapon we have in combating the accompanying bronchitis associated with so many of our tuberculous cases: and that the clearing of this complication reduces the treatment of pulmonary tuberculosis to its simplest form, namely, the disease per se.

CONCLUSIONS

1. Autogenous vaccines are indicated in a certain proportion of cases of pulmonary tuberculosis. In a series of 63 cases, 32, or 52 per cent, improved, and 15 of these were stage III cases.
2. More than one organism to a vaccine is contraindicated in most cases. Stock vaccines are useless.
3. The organism which gave the best results in the above series of cases was the Streptococcus hemolyticus.
4. Vaccines are contraindicated when there is present some evident focus of infection outside the lung. Here the course indicated is to remove the other focus and after a month or two start vaccine therapy.
5. The vaccine treatment is not suitable when there is a coexisting acute infection, an acute exacerbation of tuberculosis or persistently high temperature.

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REINFECTION IN TUBERCULOSIS

EXPERIMENTAL ARRESTED TUBERCULOSIS AND SUBSEQUENT INFECTIONS

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PART I: EXPERIMENTAL REINFECTION

THE PROBLEM

The observant student of the history of tuberculosis will be inclined to reflect that the problems concerning it have a way of recurring. After a solution has been found that seems to satisfy most if not all of the known facts, a new angle appears, or a related fact unconsidered at first opens the subject anew.

For fifty years the problem of infection has formed a conspicuous illustration of this recurrence, one of the veritable tangles among our medical mysteries. It has apparently been unravelled every ten years since Villemin's demonstration of the infectiousness of tuberculous tissue was generally acknowledged.

First was the discovery of the bacillus, then its transmission by dust as shown by Cornet in 1890, by moist droplets by Flügge and his pupils in 1900, by early childhood infection from milk by von Behring and the conflict aroused by Koch's denial of its import.

Another decade was devoted to an unprecedented research into the relationship between human and bovine tuberculosis and by 1910 the British Royal Commission and the German Imperial Commission had practically settled the question of danger from milk. Meanwhile the researches by Park and Krumwiede (1) in New York, Griffith (2) in London, Lydia Rabinowitsch (3) and Möllers (4) in the Koch Institute, have brought together an average of ten per cent of deaths from bovine infections in all cases, and these practically limited to children under fifteen years.

Simultaneously the tuberculin reactions were being widely used in diagnosis and often mistaken interpretations were made of an active tuberculosis. Lastly, the extraordinary development of the X-ray in the diagnosis of tuberculosis, especially of concealed pulmonary and healed disease, has contributed in no small degree to the reopening of the problem of infection.

The questions that have been before us during the past decade relate not only to the old problems of heredity, disposition and the channels by which the bacillus enters the human body, but also to the frequency of infection, quantity and type of bacilli, their virulence and transformations or adaptations when originating from bovine or other sources than human.

Having before us the results of painstaking observations on all these topics, we have been confronted with some contradictions.

On the one hand there is the certainty that the tubercle bacillus produces dangerous and progressively fatal disease in individuals of all ages and races and of quite vigorous constitutions.

On the other hand it causes a primary infection often, and then ceases to multiply and spread; indeed, many times multiple foci are formed which heal and persist, or ultimately disappear from individuals of even frail constitutions.

Some workers would explain all paradoxes in tuberculous infection on an immunological basis, but on careful examination we must concede many other elements in the matter.

It has seemed to us that the frequency of infection is one of the most important of modern problems in tuberculosis, and to it we have devoted our efforts in the experiments herein described.

By frequency of infection we mean the actual number of implantations of tubercle bacilli received into the body from outside sources; not the metastatic spread of a preëxisting focus of tuberculosis: in short, exogenous reinfection as distinguished from endogenous spread by any or all ways, internal or external, but originating in the individual himself.

POSSIBILITY OF EXPERIMENTAL RESULTS OF VALUE: EXPERIENCES WITH CATTLE AND NATURAL INFECTION

It may be questioned whether any attempt to imitate the natural conditions of infection in human beings can be successful. It should not be expected. The most that one could do with the present facilities in our laboratories would be to gain suggestions as to the general principles governing the facts thus far observed. It is true that cattle offer much evidence in this field under natural conditions. If it were possible to control infected cattle over a long period of years without chance of reinfection, the experiment would be yet more valuable. Unfortunately, under natural conditions in dairies, and largely because of pregnancies, infected cows develop progressive disease which usually leads to ulceration.

Even under exposure to exogenous infection it is known that many cattle slaughtered after tuberculin reactions reveal only primary foci of tuberculosis in the lymph glands, and are thus without evidence of secondary invasions.

It is, nevertheless, the opinion of authorities in veterinary science (Theobald Smith (5)), that reinfections of the lungs may occur in cows already infected elsewhere in their lymph nodes. This accounts for some instances of chronic ulcerative phthisis in cows, much resembling the human form and occurring chiefly in older cows subjected to many pregnancies and prolonged lactation in badly infected stalls.

This would seem to answer at once the question of the possibility of adult reinfection in tissues already subjected to the influence of tubercle bacilli. Moreover, there is nothing to show that adult cattle under exposure to infection for the first time possess any greater protecting factors than calves. They readily acquire a primary infection though as in man it may be quickly made inactive.

The experience already obtained with bovine vaccination against tuberculosis indicates a definite protective action for a year or two after the protective inoculation; then infection takes place as in unprotected calves. So far as these experiments relate to healed tubercles and encysted bacilli in calves, the significance appears clear that bovine tuberculosis can be acquired without arousing any latent reacting power due to the remains of the previous inoculations of human bacilli. After the period above mentioned has transpired it is known that vaccinated calves no longer react to tuberculin unless they have acquired a bovine infection, or the original vaccine was sufficiently virulent to leave behind a focus or foci still containing living bacilli.

In natural infection of human beings quite analogous conditions may be assumed: some foci are wholly obsolete and others still preserve reacting power. We cannot, however, remain content with observations on cattle.

Epidemiologic as well as clinical study presents a different picture of human tuberculosis, and the contrast between infection and disease in different races is much greater. Again, the proportion of infected adults is very great as compared with those who become actually diseased. There are no other animals which are available for the study of reinfection under natural conditions, although, theoretically, monkeys would be well adapted.[1]

Sheep, swine and rabbits are fairly resistant to human tuberculosis and rather too susceptible to bovine bacilli for primary infection to remain localized or come to a standstill.

Hence there would be the difficulty of determining the lesions of exogenous reinfection, or distinguishing them from metastases of the primary infection.

Under these circumstances, and after consideration of the difficulties, we decided to use guinea pigs primarily infected by inhalation of a human type bacillus of low virulence.

Spontaneous natural infection in guinea pigs is exceedingly rare in ordinary laboratory stock, and yet precautions in experiments of this kind need to be taken to avoid danger of such animals being included. Likewise, all chances of natural reinfection must be guarded against.

The most important point of all is the possibility of a spontaneous arrest of guinea pig tuberculosis. Skepticism on this matter would be natural; however, from certain past observations that we ourselves have made with subcutaneous inoculations of the human type of bacilli of low virulence and in small numbers, animals have appeared under favorable conditions to overcome the disease entirely. Only fibrous encapsulated lesions were found when, after several years of good health, the animals were killed or died of intercurrent disease.

Similar observations have been recorded by Römer (6) and also by Webb and Williams (7). Inasmuch as the natural lifetime of guinea pigs in captivity is barely three years, the proof of arrested tuberculosis can only be considered valid when the animals are inoculated during the first year of their life.

Another question relates to the pathway of infection. Traumatic inoculations of any kind seemed undesirable except to obtain uniform dosage. Feeding infection requires large doses of bacilli and is uncertain, but inhalation avoids these objections and more nearly imitates natural infection.

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[1] In this connection it is of interest to note that the French government has quite recently granted an island on the coast of French Guinea for the use of the Pasteur Institute for experiments on chimpanzees and apes. Prof. Calmette will undertake researches there on infection and immunity under ideal natural conditions.

REVIEW AND DISCUSSION OF PREVIOUS REINFECTION EXPERIMENTS

A comprehensive treatment of this subject would necessarily include nearly all the animal and human experiments where more than one inoculation was administered.

It would include all the attempts to test the immunity of animals vaccinated against tuberculosis where the vaccine used was a living virus capable of producing actual foci of disease, however slight. The majority of such experiments have been carried out on calves, but we also have records of some inoculations of human subjects and many upon the smaller animals. Apart from some unsuccessful attempts at human inoculation in the earlier history of tuberculosis, by Kortum and Lepelletier (8), the classical incident of the accidental inoculation of Laennec (9) on a finger from a saw cut while performing an autopsy is possibly the first authentic record of reinfection; for, being twenty-four years old at the time, he was presumably already infected elsewhere in the body. He died twenty-one years later of pulmonary tuberculosis, supposedly the result of the finger infection. This may be doubted from the views prevailing at present. Surely many such infections take place on the hands of pathologists without further harm although it is admittedly possible for them to spread.

Whether Tappeiner's (10) animal caretaker who became fatally ill from tuberculosis following exposure to sprayed sputum was an instance of exogenous reinfection we can only surmise. If so, it constitutes one of the few instances of laboratory workers whose infection could be undoubtedly traceable to carelessness and massive dosage by inhalation.

Most of the experiments of early date were made by subcutaneous inoculations and for the purpose of treatment or preventive inoculation (vaccination) against the disease. Charrin (11), for example, by reinoculating an already tuberculous animal, found that it gave a bad lesion.

Cavagnis (12) gave rabbits daily inoculations of a 0.1 per cent sputum suspension in increasing doses for twenty-seven days after the method of Pasteur. The results were of no importance, as abscesses were the chief effects.

H. Martin (13) used tubercle bacilli heated to 51.5° C. from one to five hours for a vaccine. The results were barren of protection on subsequent virulent infection; presumably the first inoculations were with dead bacilli.

Living cultures attenuated in virulence were tried upon guinea pigs by Dixon (14) early in the nineties, when Koch (15) was engaged in his classic experiments on reinoculation which led to the introduction of tuberculin. But even earlier Koch had noted in his first work on the etiology of tuberculosis (1889) while inoculating dogs in the peritoneum that one survived a primary inoculation, although it succumbed to a double dose five months later.

The secondary subcutaneous inoculation of tuberculous guinea pigs gave such a striking contrast to the first that Koch was led to follow the inflammatory effect closely, and noted the stages from the beginning of necrosis to the sloughing and healing without effect on the regional glands. This has since been known as the "Koch phenomenon." Arloing (16) and others did not succeed in confirming Koch's observations by similar attempts at reinoculation; their animals became worse and the second infection spread. Straus (17) had quite the same experience as Arloing.

Grancher and Ledoux-Lebard (18), and Hericourt and Richet (19) had published attempts in 1891 to vaccinate rabbits and dogs with avian bacilli.

Simultaneously Trudeau (20) succeeded in showing a markedly favorable influence on tuberculosis by reinoculation into the eyes of rabbits. They were first inoculated with living avian bacilli. Later he found that guinea pigs could be apparently protected against reinfection by the use of a low-virulent human bacillus for primary infection. De Schweinitz (21), using the same culture, had already noted this. Soon afterward, McFaydean (22), Pearson and Gilliland (23), von Behring and Römer (24), Theobald Smith (25), Calmette (26), and many others began the experiments on cattle immunization which were carried on so extensively between 1900 and 1910. The features of these experiments that interest us in connection with our study are the use of low-virulent human or bovine bacilli for primary inoculations and the subsequent fate of the animals exposed to natural or artificial infection, especially by inhalation and feeding.

The majority of these experiments were made with more or less virulent human bacilli which were inoculated subcutaneously or intravenously (von Baumgarten (27), Hutyra (28), Finzi (29)), and later reinoculated with bovine cultures or diseased tissue in the same way.

But few final reports of the postmortem findings have been published. Some feeding tests and inhalations were made and many animals were exposed to natural infection in stalls during the extensive trial of von Behring's Bovovaccine as a preventive. Hutyra (28) published some artificial feeding experiments in which reinfection through the digestive tract took place but with much less severity than in the controls. He also reported two inhalation experiments where the vaccinated calves escaped.

Weber and Titze (30) reinfected four calves by inhalation four and five months after vaccination and found only partly healed lymph nodes, chiefly bronchial and mediastinal, when the animals were killed seven to eight months later. The lung parenchyma was free from tuberculosis but two control animals showed extensive pulmonary tuberculosis. Under stall infection, one out of three calves remained free from disease, while the other two had less than the controls, and chiefly in the submaxillary glands. Their feeding experiments were, however, not so favorable, nor were their natural stall infections much better; for the "immunized" calves developed secondary bovine infection with one exception—but of course under extreme conditions of exposure.

The experiments of Calmette and Guérin (31), begun in 1912 and reported in 1920, are more promising for the future application of preventive inoculation.

They used their bovine culture of attenuated virulence by intravenous inoculations on 6 heifers, nine to ten months old, and exposed them for three years to natural infection under extremely unfavorable conditions. Of 4 controls, 3 became infected. Two out of 3 once vaccinated animals showed some lesions when slaughtered; 1 of the twice vaccinated and 2 of the thrice vaccinated showed no evidence of disease.

Two noteworthy facts must be considered in these reinfected calves: first, they were immature, being only four to eight months old when exposed to reinfection; second, a single subcutaneous, intravenous, ingestion, or inhalation test with virulent bovine bacilli might be resisted, while prolonged—three months to three years—exposure to badly infected stalls resulted in gradually repeated infection, notwithstanding an undoubtedly relatively higher resistance than the controls.

Immature animals may be compared to young children in their ease of infection, whereas full grown individuals have better developed physiologic defenses in the respiratory and digestive tracts.

INOCULATION OF HUMAN SUBJECTS

As already noted, it is well known that many skin inoculations on human beings fail to spread and even purposeful inoculations have been made both subcutaneously and intravenously without harm.

Baumgarten (32) is the authority for the report of an unnamed experimenter who inoculated cancer patients with bovine tubercle bacilli. Only local effects were produced. Later F. Klemperer (33) tried the same experiments on himself without experiencing harm, and thinking that bovine bacilli might favorably influence human tuberculosis he treated four patients with such inoculations. In all he gave thirty-nine subcutaneous injections of living bacilli. Local tuberculous nodules were produced under the skin and, in the larger doses, cold abscesses (four times). None of the patients was harmed and all subjectively improved. Garnault (34) is also said to have injected virulent bovine bacilli into his own forearm with no harmful result. In 1902 Alfred Möller (35) was inoculated intravenously with a small dose of living human bacilli. There was no fever reaction, and except that he lost fifteen pounds during the succeeding three months he suffered no ill effects.

Intravenous inoculations of bovine bacilli in man, without resulting harm, are also reported by Calmette (36). The culture was one of attenuated virulence and produced no infection in either calves or human beings.

The accidental inhalation without harm of millions of dry virulent bacilli by Hans Much and his coworkers in his laboratory is reported by Ritter and Vehling (37). It is a difficult matter to avoid such accidents in research laboratories where dry material is manipulated, yet to our knowledge no authentic instance of their causing pulmonary tuberculosis has been reported.

In considering these self-inoculations it must be borne in mind that they were made on adults who doubtless had already been infected in childhood. In subcutaneous inoculations with very small doses of living human tubercle bacilli Webb and Gilbert (38) found that less than ten bacilli could infect a child previously negative to a Pirquet test.[2]

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[2] It is of interest to recall the intravenous injections of tuberculin residue, known as T.R., which was made from living virulent human cultures, dried and pulverized. In the first preparations living bacilli were present and doubtless frequently injected without adding perceptibly to the tuberculosis already present in the patients.

Whatever application these experiments may have, it should be realized that infection and the relative immunity which can be demonstrated so clearly on animals has also had a practical demonstration on human subjects.

INTRAVASCULAR REINFECTION

The majority of experiments that have exhibited the phenomenon of immunity from infection in the most striking form have been done by direct inoculation into the blood stream.

The early attempts of von Behring (24) with calves were made in this way; likewise those of Trudeau (39) with rabbits. When both primary and secondary inoculations were thus given, the now familiar acute reaction was produced with pulmonary congestion and remarkable disappearance of the reinoculated bacilli after a period of from ten to twenty days. Römer and Joseph (40) made a special study of these reactions on sheep reinoculated by the vascular route. Violent febrile reaction and severe prostration followed, from which the animals recovered in three weeks. Pieces of lung taken from the surviving animals ten months later, when they were killed for comparison, were found innocuous for guinea pigs. Had the hilum glands been inoculated it may be presumed that positive results would have followed, because a few bacilli usually escape destruction.

Reinfections by the intravenous route were performed by Selter (41) with small doses of bacilli only one month after primary infection. The outcome was unfavorable, since no difference was seen between the controls and reinfected animals with respect to the pulmonary tubercles. Recently Debré and Paraf (42) tried intracardiac reinfections after primary subcutaneous infections. The reaction was strong for three to five days except in a few which failed to react differently from the controls. They lost weight, but regained it, and later developed chronic tuberculosis. The controls suffered the usual course of the disease.

Della Cella (43) used intravenous primary inoculations of virulent bacilli in very small doses, thereby producing a disease with a mild course. He reinoculated subcutaneously 10 guinea pigs after twenty days and afterward every fifteen days,—some a second or third time. Each time he produced the inflammatory reaction with rapid sloughing and healing as described by Koch. The bacilli were not found in the indurated skin.

The lesson of the bacillemia from reinfection by the blood stream is evident: the bacilli disappear and are destroyed for the most part.

SKIN INOCULATION EXPERIMENTS

Paul Römer and Joseph (44) and Hamburger (45) were the first to carefully study the question of reinfection from an experimental standpoint and to apply it to the epidemiology of tuberculosis.

The phenomenon of Koch formed the basis of Römer's first experiments; therefore he tried to reinfect guinea pigs already inoculated with weak human type bacilli in the form of von Behring's Bovovaccine. He first used bovine bacilli by subcutaneous, intraperitoneal, cutaneous and intracutaneous inoculations. With few exceptions they resisted the second infection. He concluded after some measured doses that an amount below 1000 bacilli was well resisted in the skin, but occasionally infection was produced by more.

The guinea pigs also resisted infection from tuberculous tissue removed from and reinoculated into the same animal.

While many inoculated bacilli disappeared from the skin, there were a few left sufficient to infect another animal. When the test was made by excising the skin, although they were encysted and harmless in the first animal, the bacilli were capable of infecting a healthy subject. Webb and Williams (46) injected increasing numbers of human bacilli subcutaneously into guinea pigs without infecting them.

F. Hamburger (45) also found a relative immunity to skin inoculation produced by scratching bacilli into the skin of tuberculous guinea pigs. He used small amounts, as he found that the immunity was not absolute. Later Grüner and Hamburger (47) tried a series of subcutaneous reinoculations beginning four, six, eight and ten days after primary infections. After six days the reaction to reinfection was distinct, even before any noticeable evidence of change took place at the site of the primary inoculation.

Levy (48) first infected guinea pigs subcutaneously with bacilli weakened by 80 per cent glycerol, which then gave a chronic disease. On reinfecting them in the same manner with virulent bacilli he subsequently noted cavities in their lungs similar to human phthisis.

Kraus and Volk (49) scarified the skin of apes already infected with human or bovine bacilli in the same way. They discovered that the apes were immune to reinoculation in this way, but if they used an avirulent strain for the primary inoculation, no immunity existed. This was likewise true if avian bacilli were first inoculated, as had already been found in calves.

F. Arloing and Dufour (50) found that guinea pigs could be reinfected subcutaneously up to the twentieth day after primary inoculation; afterward they were immune. The more virulent the first infection the sooner the immunity developed.

Kleinhaus (51) reinoculated guinea pigs subcutaneously on the genitalia, having inoculated them under the jaws eight to fourteen days previously. No infection followed although half of the animals showed slight swelling of the inguinal glands.

Bruyant (52) tried repeated inoculations with 5 to 10 bovine bacilli under the skin on 20 guinea pigs every two days. All became infected as with a single dose.

Löwenstein (53) reinoculated guinea pigs previously infected by intraperitoneal and intratracheal inoculations. He found a marked resistance to intracutaneous and subcutaneous reinfection.

Chaussée (54) repeated Römer's experiments but considered immunity incomplete in guinea pigs. He noted the greater destruction of bacilli and the lessened tendency to caseation in secondary foci developing from the first inoculation.

Rist, Kindberg and Rolland (55) repeated Römer's intracutaneous experiments with 32 guinea pigs with the following results: (1) 17 showed the Koch phenomenon; (2) in 4 a chancroid-like ulcer was found at the site of the inoculation; (3) in 11 a lesion resulted similar to the primary inoculation which progressed but was slightly accelerated in development. They did not employ a uniform primary inoculation method.

Siebert (56) also repeated Römer's experiments with bovine bacilli reinoculated subcutaneously from one to four months after a primary infection of low virulence. He concluded that a weak infection gave more or less protection against more severe infection, that the degree of protection depends on the kind of first inoculation and amount of the second, and that in the lungs of reinoculated animals, after severe infection, cavities appear which are not seen in the control animals.

Krause and Peters (57) more recently have studied very carefully the successive stages of intracutaneous infection and reinfection. The salient features are: (1) the immediate inflammatory reaction which is not tubercular in character; (2) the accelerated development of nodular tubercle composed of epithelioid and fixed tissue cells as seen in ordinary tubercles; (3) the abortive development of lesions in these animals due to their sensitization; and (4) the retrogression and healing of these quickly formed foci.

Krause and Willis (58) have also found a perceptible alteration of the lesion when the reinoculation was made in tuberculin-reacting skin areas, the immunity being reduced.

The cutaneous and, to some extent, the subcutaneous experiments demonstrate very well the usual course of events on reinoculation. The accelerated or inflammatory response is uniformly found in animals which have had primary inoculations of living human or bovine type bacilli. The course of the reaction depends upon the time, the dose of bacilli, and the severity of the first infection. The virulence of the reinoculated bacilli does not always seem of moment when the dosage is small; in general, it requires many more bacilli to cause the spread of a second infection than of the first, unless they follow very closely.

The time when a reinoculation is followed by an inflammatory reaction is simultaneous with the onset of skin sensitiveness to tuberculin. This varies from six days to two and one-half months after artificial and natural infection, as found by Römer (59) and Hamburger (60).

The decidedly far reaching application of the principle of autoimmunity derived from these reinoculation experiments by Römer, in relation to the dangers of reinfection from contact with tuberculous persons, brought about a change in our viewpoint as to the reason for susceptibility to infection and the opposite condition, a relative immunity. It needed more study, however, and a profounder knowledge of the pathology of the phenomenon.

REINOCULATION OF SEROUS CAVITIES

The question naturally arose whether the skin had special properties of resistance not possessed by other tissues. Römer and Joseph (61) reinoculated a few tuberculous guinea pigs intraperitoneally with bovine bacilli which, with one exception, were well resisted.

Kraus and Hofer (62) studied the "Pfeiffer phenomenon" of intraperitoneal lysis of tubercle bacilli in tuberculous animals and found that they disappeared in large numbers.

Manwaring and Bronfenbrenner (63) made a valuable study of the lysis of tubercle bacilli on various animals. They first used subcutaneous inoculations of virulent human bacilli on guinea pigs, white rats, rabbits, dogs and two monkeys. Intraperitoneal reinoculation was followed by the rapid formation of fluid exudate in guinea pigs and disappearance of bacilli to one per cent of the quantity inoculated during the first hours, and the remainder were adherent to the omentum. In the control animals fifty per cent of the bacilli remained and were well scattered. After four or five weeks they found most of the peritoneal surface of the reinoculated animals free from tubercles, while the controls were studded. They also found that fewer bacilli were destroyed where the culture was fresh and virulent. Many degenerated forms of bacilli were found which stained as Much granules. They further produced lysis *in vitro* with isolated pieces of intestine. The other animals, with the exception of the monkeys, displayed this phenomenon with less uniformity but all to some extent.

Rist, Kindberg and Rolland (64) reinoculated guinea pigs in the peritoneum and described severe reactions following the injections, from which the animals recovered after four or five hours. The bacilli were destroyed and tuberculous peritonitis did not ensue. The exudate, however, was capable of arousing a rapid peritonitis if injected into healthy pigs.

Paterson (65) reinoculated a series of guinea pigs in the pleural cavity, the primary infection being given subcutaneously in the groin and with a low-virulent human strain of bacilli.[3] The result varied with the dose of reinoculated virulent bacilli; a prompt effusion followed the larger doses (0.001 gm. to 0.0001 gm.), but only a few drops accumulated with 0.000,001 to 0.000,000,1 gm. The bacilli disappeared as in the peritoneal experiments, and those remaining appeared chiefly in the pleurae, embedded in fibrin. The fluid was virulent for healthy pigs, although bacilli were not found in some exudates taken at different periods. The adherent pleurae gradually cleared as the fibrin was absorbed and the disease spread to the lungs in a chronic form, whereas the controls developed rapid disease of both the pleurae and other organs, and in some instances late effusions.

REINOCULATION OF ORGANS

Shieck (66) found in rabbits that inoculation in the anterior chamber of one eye conferred a marked protection on the other. Krusius (67) reinoculated opposite eyes after thirty-seven days when the first eye was clinically diseased, and saw no tubercles up to thirty-six days: isolated foci were seen after sixty days by microscopic examination.

Rist and Kindberg (68) obtained evidence of an allergic reaction in the kidneys of tuberculous dogs by intravenous inoculation.

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[3] The same used in our experiments. See page 445.

Soper (69) reinoculated rabbits with bovine bacilli into the mesenteric veins, and produced secondary reactions in the liver. He concluded that the liver of a tuberculous rabbit had a very great degree of immunity to secondary inoculation, and the course of the reaction was identical with that produced in the lung. The tubercles largely disappeared in fifty to eighty-five days, although the animals killed up to seventeen days seemed to have much more disease in the liver than the controls. From the seventeenth to the twenty-sixth days rapid absorption took place.

PULMONARY REINOCULATION

Intratracheal primary and secondary injections, to produce infection in guinea pigs, were performed by Bezançon, Brunel and Serbonnes (70). They employed large doses of human bacilli and animals previously used for subcutaneous reinoculation experiments which had already shown the Koch phenomenon. The animals had severe dyspnea for the first four to seven days. The controls ordinarily died eleven to thirty-two days after such injections, whereas the allergic animals died very early (second to fifth days) or survived from one to two months. The authors contrast the primary lesions with those from the reinfection, by noting caseous bronchopneumonia in the first lesions while it was absent from the second after the allergic inflammation was absorbed. Few bacilli were found at first. Later they appeared to increase in the old lesions. The authors note that there is a direct infection of old tuberculous tissue in their experiments.

The foregoing review records the effects to be expected from traumatic reinoculation.

NATURAL REINFECTION BY FEEDING AND INHALATION

Our special interest is directed to the results of the natural and probably the most frequent ways of infection, by the respiratory tract.

The observations on calves have already been alluded to (pages 434 and 435). Römer (71) exposed old, practically healed tuberculous and healthy guinea pigs in the same cages with others which had external skin ulcers.

Out of 3 controls, 2 became infected, but none of the 4 arrested tuberculous animals acquired a second infection. These experiments were twice repeated, some of the animals receiving primary peritoneal infection. All the controls were infected in the course of six to ten months, but the previously infected animals were not. It is assumed that most of the controls were infected by licking the ulcers of the diseased, as is their wont.

Hamburger and Toyofuku (72) tried inhalations of dry room dust mixed with cultures of human tubercle bacilli, on guinea pigs which had been inoculated subcutaneously from fourteen to fifty-five days previously. They exposed 3 pigs three minutes and on examination of the lungs found so few tubercles as compared with the controls that they concluded that these could be ascribed to the primary infection.

Grysez (73) infected guinea pigs subcutaneously with bovine bacilli and after a month, when the disease had reached as far as the spleen, he gave them inhalations of bovine bacilli, and found less disease than in the controls and prolongation of life in some.

The most extensive and important work on reinfection was published in 1916 by Selter (41) while our early experiments were in progress. He employed large doses of virulent human bacilli by inhalation, after attempting by dilution and counting to determine the minimal infecting dose. In his preliminary experiments he tried intravenous, subcutaneous and intraperitoneal inoculations, but concluded that, for guinea pigs, inhalation formed a sure method of infection, even in numbers down to five tubercle bacilli.

He expressed the opinion (at which we have independently arrived) that a single living, virulent bacillus is capable of infecting a guinea pig if it gains access to the tissues of the body.

He was successful in infecting with 2 bacilli (2 out of 3 animals) subcutaneously.

The age of the culture was important as a four weeks' growth contained many more living bacilli than the eight weeks' broth culture. The dose of 100 inhaled bacilli (of four weeks' growth) was fatal on the average in eight to nine weeks, very much the same period as in subcutaneous inoculation.

In the determination of disease Selter used the intracutaneous tuberculin test and, after section of the animal, the weight of the spleen. No histologic study of tissues is mentioned.

The experiments with primary and secondary infection by inhalation are the important ones, but they are few in number. One thousand bacilli from an eight weeks' culture were inhaled for the primary infection. The secondary infection was made from a four weeks' culture in doses of 10,000 to 10,000,000, two and one-half months later, together with healthy controls. They all became infected. Other animals infected in the same way with from 100 to 1000 bacilli were reinoculated intraperitoneally, subcutaneously and intravenously with large doses. No immunity appeared. Selter found that the disease in the reinfected animals behaved very much like primary tuberculosis; that they did not show indications of immunity except in the subcutaneous inoculation area; that the primary disease did not become virulent because of reinfection, and that in general from one to two and one-half months after a weak infection he obtained little or no confirmation of Römer's experiments.

He admitted that a longer period was required to permit the first infection to come to a complete standstill, and he failed to use the tuberculin test before reinoculation to determine this point satisfactorily.

The virulence and dosage of the bacilli were evidently too strong for guinea pigs, and the result could hardly have been otherwise than unfavorable in showing immunity from infection, since it was progressive from the first.

PLAN OF INHALATION REINFECTION EXPERIMENTS

It was our plan to produce if possible a completely arrested tuberculosis before attempting reinfection.

This point seemed important, and indeed necessary, if we should be able to prove exogenous reinfection.

We know from a study of tuberculosis in the guinea pig how uniformly the tracheobronchial nodes become diseased from whatever avenue the tubercle bacillus enters. In our experience ordinary human tubercle bacilli seldom fail to grow in the animals, however slowly the disease may appear to progress. Often a very sleek, well nourished animal appears to have recovered after six to eight months, only to emaciate gradually, lose his perirenal fat, develop dyspnea from gradual consolidation of the lungs, and finally die from the disease or some complication.

There are cultures, however, of both human and bovine origin, that by artificial cultivation have acquired low pathogenicity for guinea pigs. Such have been described by several workers in tuberculosis, notably Trudeau (74) and Calmette (75).[4]

[4] These types are not to be classed with bacilli passed through cold blooded animals and alleged to be transformed thereby (Klimmer (77), Friedmann (78) et al.). No proof has been brought that these were derived from human bacilli; they are undoubtedly simply saphrophytic acidfast bacilli commonly found in batrachians.

Having had a long experience with the culture isolated by Trudeau in 1891, which has been extensively used in this country in immunity experiments, it was natural that we should employ it in these experiments. Krause (76) has given a good history of it in a recent article in this journal, in which the statement is made that the inoculation of R1 results in a limited disease of the lymph nodes, seldom or never becoming generalized. We shall note (pages 454 and 455) in the inhalation disease that a few animals ultimately develop chronic generalized tuberculosis, though practically all escape without lesions extending beyond the lungs and tracheobronchial glands. The exceptions led us to suspect that an accidental mixture with a virulent strain of bacilli had been inoculated into these animals.

As will be noted on page 458 we were unable by passage experiments to confirm this idea, but concluded that R1 was not invariably weak in infectivity.

It must be confessed that guinea pigs confined for many months in cages were good subjects for spontaneous infection, yet none such were recognized in our experiments.

We feared to use young animals for this work lest even the weakest bacilli might have too strong an invasive power, and therefore chose nearly full grown guinea pigs weighing from 300 to 500 grams and from eight to twelve months old.

To obviate so far as possible the danger of introducing spontaneously infected animals we gave all animals at the start an intracutaneous test of 0.02 cc. of old tuberculin in 0.1 cc. injection.

Males were used for the most part, as they are stronger and complicating pregnancies were not desired.

Half of the animals of our first series were kept as uninoculated controls in cages alongside the others.

Objection to the value of the intracutaneous test when resulting negatively in the guinea pigs is of course readily admitted; it cannot possibly exclude infection any more than in human subjects, but it was deemed the best index in our possession during the life of the animal. The presence of a small focus of inactive disease is not certain to be revealed, yet seldom could there be such an inactive focus in spontaneous infection of the susceptible guinea pig.

DOSAGE OF BACILLI: DUST INHALATION METHODS

Mention has been made of the intention in these experiments to approach as nearly as possible natural conditions of infection. To this end we tried both dried and moist bacilli, and at first we made use of various contrivances to give a small dose of finely powdered bacilli. To avoid clumps of several hundred bacilli, which become agglutinated in drying, they were rubbed in a glass mortar and blown from the bottom of a tall (one metre) glass cylinder by a compressed air blast. The outlet tube at the top was plugged with glass wool. Only the slightest particles were carried over, yet many clumps were found on stained slides placed in the inhaling chamber. A long spiral of glass tubing partially plugged with glass wool was then interposed between the cylinder and the delivery tube. This gave little if any better results. The counts of bacilli showed clumps of ten to fifty, besides numbers of smaller clumps. Other details of these inhalations are given in the notes of the first series. We later abandoned the dry method for the moist vapor, and as will be shown, more uniform infections were then obtained.

In Nenninger's (79) inhalation experiments with dried Bacillus Megatherii, to show how deeply bacteria penetrated into the normal lungs, he secured rather fewer colonies than from moist spray inhalations. He thought this due to the larger particles catching in the upper air passages.

Owing to the low virulence of R1 broth cultures that we used, the actual dosage was felt to be of less importance than uniform infections, and these seemed to be impossible to obtain by the use of dry material.

Nevertheless, we determined to use both methods for infection, and a sufficient number of animals to neutralize any minor differences.

Experience has shown that simultaneous infection may take place from inhaled and swallowed bacilli, particularly when the bacilli enter through the open mouth. We sought to minimize this possibility by confining the animals during the process in rubber cones made from the inner tubes of automobile tires, a small opening at the apex permitting easy breathing but effectually closing the mouth of the animal. This method also served to protect the hair of the body from infected dust and vapor, only the nose requiring disinfection after exposure in the experimetal infection.

After being clamped in the rubber cones, some animals were placed in a box and the air stream from the dusting cylinder was directed into the box through an opening facing the protruding noses of the guinea pigs.

This method gave uncertain degrees of infection, and occasionally none.

Eventually we held each animal separately in the left hand (covered with a rubber glove) 6 inches (15 cm.) away from the outlet of the dust cylinder, as seen in figure 1. The operation was of course performed in a laboratory hood with a good chimney draft, to protect the operator. With these precautions the results became more satisfactory.

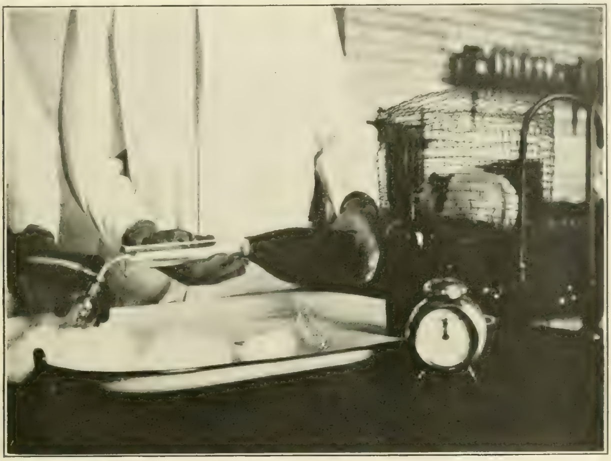

FIG. 1. METHOD OF INFECTION BY INHALATION OF SPRAY

RECORDS OF EXPERIMENTS

Series 1: *Experiment 356*:

Primary inhalation R1, low virulent culture, dried.

Secondary inhalation H51, highly virulent culture, dried; one year later.

On November 22 to 25, 1916, intradermic tuberculin injection of 0.2 cc. O. T. in 0.1 normal saline solution was given to 50 guinea pigs of 500 to 750 grams weight. None reacted in forty-eight hours. After one month they were separated and a portion inoculated. On December 29 and 30, 1916, 24 healthy pigs were given an inhalation of R1 broth culture, fifteen-day fresh growth from the edge of the pellicle, dried fifteen hours over sulphuric acid in a vacuum desiccator at 24° to 48°C. and protected from light, then pulverized in a glass mortar. The animals were exposed for thirty seconds to a blast in the manner already described, at a pressure of fifteen pounds in the air tank. The dose blown from the cylinder was estimated at 0.005 gram at each blast. Only a small portion of this was inhaled by the animals.

Tuberculin tests of 0.02 cc. intracutaneously were made after one, six, seven, eight, and eleven months. The positive results are shown in table 1.

Note may be made that two-thirds of the guinea pigs reacted at the end of one month and three-fourths of them at the end of two months, while later the reaction became weak and after eleven months the survivors lost their reaction power.

Fourteen remained after a year, the others having died from various accidents and diseases, principally chronic indurative pneumonia which involves the small lobes of the lungs and is quite prevalent in old guinea pigs. Tuberculosis in the tracheobronchial nodes was demonstrated in three of those sectioned among the early deaths; in one no disease was found.

The surviving animals appeared in perfect health, and it was reasonable to consider the tuberculous group as well arrested or not infected—where a negative tuberculin test occurred during the first months. A few infected animals had been kept for controls, but of these only two remained and were given the virulent inhalation. The others had been used for different purposes.

On November 17, 1917, approximately one year later, 10 of the infected animals and 2 controls, together with 6 new healthy control pigs, were given the virulent inhalation. For fifteen seconds they inhaled dried H51 (fifteen-day broth culture recently isolated from sputum, the fourth transfer from egg tubes), approximately 0.019 gram in each blast. Two animals of the first infection series were reserved for controls and for comparison with the reinoculated ones.

Table 1 contains the records and clearly indicates the markedly smaller amounts of disease in the guinea pigs twice infected and chloroformed after ninety-three to one hundred and one days, although in animals 22 and 24, killed after one hundred and fifty-one days there was practically as much disease as in the controls.

The intradermic tuberculin tests on the tenth day after infection gave no response in either first or second inoculated animals. On the forty-first day after the virulent infection all but one control gave strong reactions, while only three of the reinoculated pigs reacted definitely. This difference will be discussed later and its significance noted.

Differences in the tuberculin reactions made it seem likely that there were some of the original animals which escaped infection. Histologic examination in five had failed to discover tubercules; consequently we made some secondary inoculations of suspected lung and gland tissue from both reinoculated and

TABLE 1A

Series 1. Reinfection: Virulent inhalation H51 dust; after 11 and 12 months

ANIMAL NUMBER	WEIGHT AT DATE OF		INTRADERMIC TUBERCULIN TESTS				TOTAL DURATION OF LIFE SINCE	
	First infection	Second infection	Five tests 0.020 cc., number positive reactions after first infection	0.020 cc. 9 days before second infection	0.020 cc. 10 days after second infection	0.020 cc. 41 days after second infection	First infection	Second infection
	grams	*grams*					*days*	*days*
*11	520	610	0	0	+?	0	414	94
12	700	780	1	0	0	0	422	101
13	630	690	3	0	+?	+?	422	101
16	560	675	2	0		+++	414	93
17	630	655	1	0		+++	414	93
18	650	680	1	0		0	422	101
19	525	600	1	+?		+?	414	94
21	595	640	2	0		+++	414	94
22	740	710	2	+?		++55days	505	151
24	610	610	1	0		+? 55 days	505	151
Controls—not reinoculated								
25	710	570	1	0			505	
28	700	815 When killed	2	+?		+?	507	

*The first ten animals were used for other experiments.

Key to tables

Tuberculosis on gross examination	+
Tuberculosis with caseation on gross examination	++
Tuberculosis on histological examination Tuberculosis with very early proliferation	T_1
Tuberculosis with advanced proliferation	T_2
Tuberculosis with early caseation	T_3
Tuberculosis with advanced caseation	T_4
Tuberculosis with early healing	HT_1
Tuberculosis with advanced healing; fibrous	HT_2
Tuberculosis with allergic reaction, early	A_1
Tuberculosis with allergic reaction, retrograde	A_2
Lymphoid hyperplasia	L
No specific tuberculous lesion	0

Note: The tuberculin reactions are indicated according to severity from + to ++++.

control animals (see table 1, control). We tried to distinguish in this way by the virulence of the tuberculous tissue which lesions were due to the first inoculations and which to the second. In no. 25 R1 control it will be noted that the lung tissue was not able to infect but the lung hilum lymph node was positive after two months; whereas no. 96, the H51 control, promptly gave a progressive disease to two healthy pigs.

TABLE 1B

Series 1. Controls: Virulent inhalation H 56 (dust)

ANIMAL NUMBER	WEIGHT			TUBERCULIN TESTS	
	At date of infection	Maximum after infection	Minimum after infection	10 days after infection	41 days after infection
93	760	780	–	0	++++
94	500	580	–	0	+++
95	340	420	420	0	++
96	490	525	420	–	++++
97	460	520	450	–	++++
*98	400	550	520	–	0

Control of virulence of tubercles from reinoculated animals

		TISSUE INOCULATION	NUMBER OF ANIMAL	VIRULENCE	
				Weak	Strong
109	410	Bronch. nodes	25 control	+	0
110	350	Lung tubercle	25 control	0	0
111	420	Lung tubercle	11	0	0
112	375	Lung tubercle	11	0	0
113	460	Lung tubercle	96		+
114	340	Lung tubercle	96		+
116	400	Lung tubercle	21	+?	+?
117	310	Lung tubercle	68		+
118	425	Spleen	68		+
119	300	Lung	13		0
120	420	Lung	18		+

(*98 probably escaped infection.)

The lung nodules of no. 11 and no. 13 were both negative on inoculation. These require special mention, as the small grayish or pearl-like nodules that were inoculated proved on histologic examination of similar foci to be the nonspecific lymphoid hyperplasia which will be discussed later (see page 472). There were larger nodules in the subpleural region containing giant cells but no caseation. In both animals there were well defined tubercles in the bronchial lymph nodes which would probably have produced infection by inoculation, but this was not done in all cases. Bacilli were not found in the sections, however, nor in the lung tubercles in a casual search. The small

TABLE 1c

Series 1. Reinfection: Virulent inhalation H 51 dust; after 11 and 12 months

ANIMAL NUMBER	GROSS AND HISTOLOGICAL EXAMINATION OF TISSUES						
	Lungs; Lesion from		Cervical Tracheo-bronch. lymph glands	Axillary Inguinal lymph glands	Spleen	Liver	Complications
	First infection	Second infection					
11	+?	0	+ +	0 +	0	0	
12	+ L	+ T_4	+ +	0 +	+	0	
13	0 L	T_2	+? HT_2	0 0	+?	0	Pneumon.?
16	+?	+	0 +	0 +	+	0	
17	+?	+	0 +	0 0	+	+	Pneumon.
18	+	T_4	0 T_4	0 0	0	0	
19	0 L	0	0 T_4	0 0	0	0	
21	+?	+	0 +	0 0	0	0	
22	+?	++	0 ++	+? +	++	+	
24	+	++	0 ++	0 0	++	+	
Controls—not reinoculated							
25	0	0	0 0	0 0	0	0	
28	+?	+?	+ +	+? +	0	0	

lung nodules of no. 18 and no. 21 gave a positive inoculation disease of apparently average virulence. It was not possible to say whether these tubercles in the lung came from both the first and second infections, but presumably they were from the latter. It is noteworthy that the virus must have been weaker or the bacilli in the tissue less numerous than in the control no. 96.

TABLE 1D

Series 1. Controls: Virulent inhalation H56 (dust)

ANIMAL NUMBER	DURATION OF LIFE days	LUNGS	CERVICAL TRACHEO-BRONCH. GLANDS	AXILLARY INGUINAL GLANDS	SPLEEN	LIVER
93	91	++	+ ++	+? +?	+	+
94	91	++	+ ++	0 0	++	+
95	99	++	+ ++	+ +	++	++
96	92	++	++ ++	++ ++	++	++
97	99	++	+ +	+ +	+	+
98	99	0	0 0	0 0	0	0
Control of virulence of tubercles from reinoculated animals						
109				+		
110				0		
111				0		
112				0		
113				++		
114				++		
116				+		
117				++		
118				++		
119				0		
120				+		

Series 2: Experiment 356:

Owing to the expected high mortality in experiments with animals under long confinement, we followed our first series with others within two months. In selecting the guinea pigs we had decided, as previously stated, to use males as far as possible, and of mixed colors, obtaining them from different dealers. It was found difficult to secure older animals free from occasional traces of chronic pneumonia involving the small mesial lobes By quarantining for two weeks, the most seriously affected animals could be suspected and killed; many, however, of the best nourished ones appeared to be immune or to have recovered. The cages were of open wire on all sides and each contained not more than five animals, the sexes separated, uninoculated pigs on the upper tiers and quarrelsome males placed in solitary confinement. No ulcerating tuberculosis was permitted to remain in the animal room.

The feeding was done but once a day, exclusively on hay and carrots in winter, with green grass, oats, hay and occasionally cabbage in summer. The cages were kept dry. Water was not given except sparingly in summer, as deaths from enteritis are hard to prevent.

Primary inhalation R1, both dried and moist, February 15 to 22, 1917.

Secondary inhalation H51 (virulent) dry, November 17, 1917, nine and one-half months later.

Eight tuberculin tested pigs were subjected to inhalation on February 15, 1917, and 11 nontested ones[5] on February 22nd, 1917.

The latter were young and mostly males.

Dried and pulverized R1 culture, fourteen-day growth on broth, was inhaled for thirty seconds by the first 8 and for fifteen seconds by the succeeding 11. In addition to the above, 4 old subcutaneously inoculated animals were given inhalations with the first 8. Those animals, with controls, which survived and were reinoculated, are given in table 2.

Only 6 of this series survived until given the secondary inoculation of dried and pulverized bacilli from a twenty-six day broth culture of H51 virulent strain. The same method and time (fifteen seconds) were employed as in the first series.

Two healthy animals, not previously inoculated, had been kept side by side as controls.

Three of the tuberculous with the 2 controls were given inhalations on November 17, 1917, and the other 3 with 10 new controls on February 22, 1918, but with moist spray of a suspension of H51, twenty-seven-day broth culture in normal saline solution. This was vaporized in a DeVilbiss atomizer and four blasts were given to each pig through a glass tube 4 inches long and one inch in diameter, which was placed near the animals' nose.

The suspension was made from a large spadeful of culture rubbed in a mortar in 40 cc. of normal saline solution and centrifugated ten minutes. The middle layer, pipetted out, was used. Smears showed an average of a single bacillus to an oil immersion field. The atomizer produced an exceedingly light cloud.

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[5] No further preliminary tests of guinea pigs in stock were made, since we had previously secured only negative results.

TABLE 2A

Series 1. Reinfection: Virulent inhalation H 51 (dust) after 11 months November 17, 1917.

ANIMAL NUMBER	WEIGHT		INTRADERMIC TUBERCULIN TESTS			TOTAL DURATION OF LIFE SINCE	
	At time of first infection	At time of second infection	0.020 cc., number of positive reactions after first infection	0.020 cc. 9 days before second infection	0.020 cc. 41 days after second infection	First infection	Second infection
62	335	580	1	0	–	376	101
65	330	625	1	0	–	376	101
68	560	625	1	0	–	373	98
Controls: Virulent inhalation H51 (dust), November 17, 1917.							
74	485	670		0	+++	376	101
76	625	860		0	++++	374	101
Reinfection: Virulent inhalation H51 (moist vapor) after 12 months, February 16, 1918							
27	590	630	2	+?	55 days ++	505	90
29	560	610	1	+?	55 days +?	505	90
51	280	670	1	+?	55 days ++	509	60
54	390	780	2	+	+	395	13
55	335	620	2	0	++++	509	60
Controls: Virulent inhalation H51 (moist vapor), February 16, 1918							
		min wt.					
99	490	480	No tests	No tests	No tests		58
100	480	470	No tests	No tests	No tests		58
101	610	575	No tests	No tests	No tests		58
102	550	530	No tests	No tests	No tests		58
103	490	490	No tests	No tests	No tests		58
104	540	490					58
105	480	480					58
106	560	470					57
107	480	390					56
108	500	500					58
Subcutaneous controls: Reinfection by R1 (dust) inhalation after 1 or 2 years							
36	750	630	1?	0	+?	422+	374
37	800	740	2	–	++	508+	426
45	800	820	0	0	++	508+	426

From two to five months after virulent infection the animals of both series were chloroformed and compared. The marked difference in the amount of disease is apparent from the tables and is indicative that the arrested disease in the reinoculated pigs served to restrain, if not to prevent, acute and extensive disease. It seemed clear to us that the first infection was quite arrested in the few survivors. The greater uniformity of lesion produced by moist vaporized bacilli determined us to abandon dust inhalations in future experiments.

TABLE 2B

Series 1. Reinfection: Virulent inhalation H51 (dust) after 11 months, November 17, 1917

ANIMAL NUMBER	LUNGS; LESIONS FROM		GROSS EXAMINATION				
			Lymph glands				
	First infection	Second infection	Cervical / tracheobronchial	Axillary / inguinal	Spleen	Liver	Complications
62	+?	++	? / ++	0	+	+	0
65	+?	++	? / ++	— / +?	+	+	0
68	+?	+	? / ++	0	+	0	0
Controls: Virulent inhalation H51 (dust), November 17, 1917							
74		++	+ / +	+ / +	+	+	0
76		+	+ / +	+ / +	+?	+	0
Reinfection: Virulent inhalation H51 (moist vapor) after 12 months, February 16, 1918							
27	+?	+	0 / ++	0 / 0	++	0	
29	+?	++	0 / +	0 / 0	++	++	
51	+?	++	0 / +	+?	+	+?	0
54	0	0	0		0	0	Pneumonia.
55	+?	++	0 / +	+?	++	++	0

TABLE 2B—*Continued*

ANIMAL NUMBER	LUNGS; LESIONS FROM		GROSS EXAMINATION				
	First infection	Second infection	Lymph glands: $\frac{\text{Cervical}}{\text{tracheo-bronchial}}$	Lymph glands: $\frac{\text{Axillary}}{\text{inguinal}}$	Spleen	Liver	Complications
Controls: Virulent inhalation H51 (moist vapor), February 16, 1918							
99		++	$\frac{+}{+}$	$\frac{+}{+}$	++	++	
100		++	$\frac{+}{+}$	$\frac{+}{+}$	+	+	
101		++	$\frac{+}{+}$	$\frac{+}{+}$	+	+	Healed pneumonia
102		++	$\frac{+}{+}$	$\frac{+}{+}$	++	+	
103		++	$\frac{+}{+}$	$\frac{+}{+}$	+	++	
104		++	$\frac{+}{+}$	$\frac{+}{++}$	+	+	
105		++	$\frac{+}{+}$	$\frac{+}{++}$	+	++	Pneumonia?
106		++	$\frac{+}{+}$	$\frac{+}{+}$	++	++	
107		++	$\frac{+}{+}$	$\frac{+}{++}$	++	++	
108		++	$\frac{+}{+}$	$\frac{+}{++}$	+	++	
Subcutaneous controls: Reinfection by R1 (dust) inhalation after 1 to 2 years							
36	++	+?	$\frac{++}{++}$	$\frac{++}{+?}$	+?	+?	Pneumonia
37	0	0	0	0	0	0	
45		$\frac{A_2}{++}$	$\frac{++}{++}$	$\frac{+}{+}$	T_2	+	

Three of the 4 old pigs (supposedly) inoculated subcutaneously survived and were killed thirteen and one-half months after reinfection by R1. Two revealed chronic tuberculosis of lungs and lymph nodes, and the third (no. 37) showed none, although it had apparently reacted to tuberculin according to the notes; no microscopic examination was made.

SUMMARY OF ANIMALS OF THE FIRST AND SECOND SERIES DYING FROM ACCIDENT OR COMPLICATIONS PREVIOUS TO THE TIME OF SECOND INFECTION

Of a total of 32 animals dying from twenty-three to three hundred and fourteen days after infection at least one of the organs of 18 was submitted to histologic examination. In every instance, in spite of complicating disease, tubercles in varying stages of development were detected somewhere in the body of the animal. The lungs, examined in 7 cases, showed tubercle in 4, and persistent lymphoid hyperplasia in 3. A complicating pneumonia does not preclude the formation of inhalation tubercles. The tracheobronchial lymph nodes were examined in 14 cases, and all showed tubercles in varying stages of activity. In addition, macroscopic observation showed tubercle in the spleen 15 times (3 of these verified microscopically), in the liver 10 times and in the cervical lymph nodes 7 times.

Lesions developed in spite of complications but their course, both for this reason and because of possible irregularities of dosage, was irregular.

Series 3 : *Experiment 356* (*a*):

Primary inhalation R1, moist vapor, October 17, 1917.

Secondary inhalation R1, moist vapor, eighteen months later.

Six guinea pigs were given inhalation of R1, ten-day broth culture, in moist spray in the manner above described. The suspension contained many single bacilli and small clumps in the test smears. The animals received a fairly strong infection but apparently completely recovered after a period of losing weight. One was inoculated in the groin for control of the virulence.

Reinoculation by inhalation was made with the same strain, R1, sixteen-day broth culture, prepared in the same way. Six blasts of the vaporizer were used, there being 5 healthy animals inhaled for controls at the same time.

Notes on table 3:

We have here an interval of eighteen months between infections of like virulence. All the reinoculated animals had pulmonary lesions as well as lymph node disease, but it was not easy to state from gross appearances that these tubercles were recent; the larger tubercles and caseation present in the lungs of the controls, however, were perfectly plain by contrast. The fibrous appearance of the glands of the reinoculated animals suggested well arrested disease.

Virulence of R1 culture:

During the time the first two series of experiments were in progress, we began others with the use of larger doses of R1 powder and longer exposures. The animals were confined in a box while inhaling the powder, and in most cases the result was a rather severe infection of the lungs. Many of these animals died, and in 5 instances among 40 guinea pigs the disease had spread to the spleen and liver.

This observation raised the question whether the R1 strain had become mixed with one more virulent, or was gaining in parasitic power. We therefore inoculated subcutaneously 2 guinea pigs with a mixture of crushed lung and mesenteric gland tissue of one (no. 16a) which had died with extensive disease of the lungs and glands thirty-one days after inhalation.

TABLE 3A

Series 2. Reinfection: Low virulent R1 inhalation (dust and moist vapor) after 18 *months.*

ANIMAL NUMBER	WEIGHT AT DATE OF		INTRADERMIC TUBERCULIN TEST 49 DAYS AFTER FIRST INJECTION	DURATION OF LIFE SINCE		LUNGS; LESIONS FROM	
	First infection	Second infection		First infection	Second infection	First infection	Second infection
				days	*days*		
24	460	680	++		(No record)		
25	475	830	++	628	115	+	+?
26	440	880	+	628	115	+	+?
27	425	755	+	628	115	+	+?
38	430	785	0	632	115	+	+?
Controls: Second inhalation R1 moist vapor							
32	620	620			115		++
34	655	655			115	–	+
35	645	645			115	–	T_4
36	630	–			115	–	++
37	580	630			115	–	+
Control of virulence of tissue, first infection; subutaneous inoculation lung and gland tissue no. 16							
39	320	580			409	0	–
40	370	820	25 days +++		569	0	0

The secondary passage inoculation caused only localized lymph node disease, which became apparently arrested and fibrous. Only the inguinal nodes nearest the site of inoculation were found caseated. One pig was killed in thirteen and one-half months, the other in eighteen and one-half months. We were consequently inclined to account for the apparent accession of virulence in series 2 by the poor condition of the inoculated animals, some of which were barely half grown. Added to this, large doses of bacilli, which sometimes

TABLE 3B

Series 2. Reinfection: Low virulent R1 inhalation (dust and moist vapor after 18 months

ANIMAL NUMBER	GROSS AND HISTOLOGIC EXAMINATION OF TISSUES				
	Lymph glands			Spleen	Liver
	Cervical/Tracheobronchial	Axillary/Inguinal	Mesenteric		
24	—	—	—	—	—
25	+/+	+?/+			
26	+/HT_2	+/+			
27	+/+	+/+			
38	+/+	+/+	+	+	
Controls: second inhalation R1 moist vapor					
32	+/++		0	0	0
34	+/++		0	0	0
35	No record		—	—	—
36	+/++		0	0	0
37	+/++		0	0	0
Control of virulence of tissue, first infection: Subcutaneous inoculation lung and gland tissue no. 16					
39	+/+	+/+++	+	0	0
40	+	+/+++	0	++	+

contained clumps, were administered. In fact we began to note that infection by inhalation appeared to be more serious in its effects than subcutaneous inoculation, with the R1 strain of bacilli.

This became more pronounced in later experiments with moist spray, containing relatively many less bacilli than we usually gave under the skin.

As a consequence a further control test of the virulence of the R1 culture was made to allay suspicion of its change or mixture with more virulent strains (see table 5).

Series 3: *Experiment 356* (*b*):

Cumulative infections by three successive inhalations.

R1 moist vapor
- 1., December 7, 1917.
- 2., August 19, 1918, eight months and twelve days later.
- 3., February 12, 1919, five months and twenty-four days later.

The object in view in this series was to note the effect of successive inhalations in moderate doses of R1 culture which, when inhaled from vaporized suspensions, had been found capable of producing a mild but fairly extensive disease in a small percentage of animals.

The experiment was begun with 26 male pigs, well grown. Six were reserved after the first infection for comparison, and with each successive infection 6 new pigs were given inhalations, making 36 in all. The suspensions were prepared as described in series 2, and tests were made by spraying against glass slides, which showed after staining from two to three bacilli to the field. Four blasts with the hand bulb vaporizer, requiring two seconds to each squeeze, were made for each animal in the manner already described. Six blasts were given in the third infection. Seven pigs received the three infections, 6 received two and 5 only the last.

They were chloroformed in two lots of 7 each at the end of one month and three and one-half months respectively, and comparisons were made by both gross and microscopic examinations. Table 4 contains the record.

Result: All the thrice inhaled pigs had enlarged and fibrous cervical and tracheobronchial nodes and a few fibrous subpleural tubercles in their lungs. Gross evidence of tuberculosis was more marked in the animals which received the last two infections, and in the controls which had only the final inhalation.

A control inoculation of the sprayed suspension, used in the third inhalation February 12, 1919, was made to test the virulence by subcutaneous injection into each groin of a guinea pig (356 x table 5). Section showed proliferative caseous tuberculosis of the inguinal nodes and spleen after three and one-half months. Evidence of an abnormal virulence for R1 was not apparent.

(A pathological study of 10 of the twice and thrice inoculated pigs is given on pages 472 ff and a summary of the sequence of changes is appended by Dr. Gardner.)

Virulence test of R1 culture by passage and subsequent inoculation:

One of the twice infected pigs (31b) died from generalized tuberculosis on February 6, 1919, one hundred and eighty days after inhalation of R1 spray. Secondary subcutaneous inoculations of spleen, liver and inguinal glands tissue of pig 31b were made into three pigs. The spleen inoculated animals died of generalized tuberculosis in seven months; the liver pig in eleven and one-half months. The gland tissue pig died in eleven days of septicemia.

TABLE 4A

Series 3. Cumulative infections by inhalation: Low virulent R1 moist vapor

ANIMAL NUMBER	WEIGHT AT DATE OF				INTRADERMIC TUBERCULIN TESTS	
	First infection	Second infection	Third infection	Death	0.020 cc. 31 days after first infection	0.005 cc., 19 days after second infection
3	375	580	580	640	+++	++++
4	355	570	605	700	+	+++
10	360	580	645	645	++	++++
11	360	600	745	810	+++	++++
17	365	670	815	835	+	–
18	345	680	735	800	++	++
20	445	700	665	740	+	?
21	410	–	740	760	++	+
22	460	–	860	910	++++	–
24	340	–	770	770	+++	–
27	–	610	–	900	–	+++
28	–	700	–	830	–	+++
29	–	780	–	800		++++
32	–	–	620	720		
34	–	–	655	790		
35			645			
36			630	705		
37			580	620		

Seven pigs were inoculated subcutaneously at the same date (February 6, 1919) with 0.1 cc. of a coarse suspension of R1 broth culture of ten days' fresh growth (the same which was used ten days later for the third inhalation). Table 5, control, shows the result in detail.

Notes on subcutaneous control inoculations of R1 culture:

A glance at the table 5 controls indicates the possibility of producing generalized tuberculosis with slight caseation with R1 after many months. The occasional instance of such extensive disease from our inhalation infection was not surprising if the dosage was large, and we cannot find sufficient ground for the suspicion that we were using a mixed culture since these instances were exceptional. On the other hand, it cannot be maintained that R1 was so weak in pathogenic properties that the value of the experiments was vitiated.

The case of guinea pig 31b is not clearly explained, as the passage inoculations proved fairly virulent. As this was the only animal among 36 to show gross evidence of spleen or liver involvement, we must suspect that it was misplaced in a wrong cage and had been previously inoculated with another strain than R1.

TABLE 4B

Series 3. Cumulative infections by inhalation: Low virulent R1, moist vapor

ANIMAL NUMBER	DURATION OF LIFE AFTER		HISTOLOGIC EXAMINATION OF TISSUES				
			Lungs; lesions from		Tracheo-bronchial lymph nodes		Complications
	First infection	Last infection	First infection	Second infection	First infection	Second infection	
	days	*days*					
3	520	26	L, HT_2	A_1	HT_2	0	
4	492	26	L, HT_2	A_1	0	T_2	
10	492	26	L, 0	A_2	HT_2	0	
11	492	26	0	T_3	HT_3	T_1	
17	548	115	L, HT_1	A_2	HT_3	—	
18	446	5	—	—	—	—	Pneumon.
20	—	(Lost)	—	—	—	—	
21	548	11	L	0	HT_2	0	
22	548	115	L, HT_2	0	HT_2	0	
24	548	115	L, HT_2	A_2	HT_2	0	
	Second infection						
27	279	26	—	—	—	—	
28	279	26	HT_2	A_2	0	0	
29	279	26	HT_2	A_3	0	0	
32		115	—	—	—	—	
34		115	—	—	—	—	
35	Died (no record of autopsy)						
			(A_1)				
36		115	L, HT_2	—	0	T_1	
37		115	—	—	—	—	

Series 4: Experiment 356 (c):

Inhalation of R1 dried, followed by inhalation of granite dust, December 10, 1917.

This experiment formed a part of the study of the effect of mineral dusts on tuberculosis carried on by Dr. Gardner (see AMER. REV. TUBERC., 1920, iv, 734). There were 13 guinea pigs of which 5 inhaled granite dust beginning ten and one-half months after infection and continuing for eight months. Only 3 control animals lived through the experiment, which was terminated June 11, 1919, eighteen months after the infection. Healed fibrous cervical and tracheobronchial nodes were demonstrated, together with a few fibrocaseous lung tubercles. The animals which had inhaled granite dust exhibited foci which were larger but not progressive (see Gardner, loc. cit.)

TABLE 5A

Series 3. Virulence test R1 culture by subcutaneous inoculation

ANIMAL NUMBER	WEIGHT AT DATE OF INOCULATION	INOCULATED MATERIAL	DIED (D) OR KILLED (K)
356×	—	5 cc. normal saline into which six blasts were sprayed of R_1 suspension	D
1×	330		K
2×	380	0.1 cc. coarse suspension of ten-day broth culture R1	D
3×	390	0.1 cc. coarse suspension of ten-day broth culture R1.	D
5×	405	0.1 cc. coarse suspension of ten-day broth culture R1.	K
6×	450	0.1 cc. coarse suspension of ten-day broth culture R1.	K
7×	430	0.1 cc. coarse suspension of ten-day broth culture R1.	K
		Inoculated material (R1 first passage from guinea pig)	
8×	400	Crushed spleen pulp no. 31 B. 5½ months after inhalation of R1.	K
9×	330	Crushed inguinal gland pulp no. 31 B.	D
10×	380	Crushed liver pulp no. 31 B	D
11×	—	Crushed spleen pulp no. 7× (above)	D
*12×	—	Crushed lung 1 cc. in each groin 5 days after subcutaneous inoculation of R1	K
13×	—	Crushed lung 1.5 cc. in each groin 12 days after subcutaneous inoculation of R1	K
14×	—	Crushed lung 1.2 cc. in each groin 18 days after subcutaneous inoculation of R1	K
15×	—	Crushed lung 2.5 cc. in each groin 28 days after subcutaneous inoculation of R1	K
16×	—	Crushed lung 2.5 cc. in each groin 39 days after subcutaneous inoculation of R1	K
17×	—	Crushed lung 1.5 cc. in each groin 94 days after subcutaneous inoculation of R1	K
18×	—	Crushed lung 2 cc. in each groin 94 days after subcutaneous inoculation of R1	K

*Animals 12× to 18× inclusive are from another experiment. Though the amount of fluid varies in each case it represents the entire amount of fluid used in crushing the whole left lung of the first animal, previously infected in the groin with 0.5 cc. of a suspension of R1 containing 3 to 5 single bacilli to an oil immersion field.

Series 5: *Experiment 356* (*d*):

Primary inhalation of R1 moist vapor, December 22, 1917.

Secondary inhalation of R1 moist vapor December 22, 1919, two years later.

This experiment was begun with 20 guinea pigs of which 9 survived two years. (There were 7 more given inhalations at the same time for the above mentioned granite dust experiment.)

The culture used was older than in series 3 (thirty-seven days), and a test of the suspension on stained slides showed many vacuolated bacilli. The inhalation was made with four blasts of the atomizer.

TABLE 5B

Series 3. Virulence test of R1 culture by subcutaneous inoculation

ANIMAL NUMBER	DURATION OF LIFE	GROSS AND HISTOLOGIC LESIONS				
		Lungs	Lymph glands		Spleen	Liver
			Inguinal	Others		
	days					
356×	–	0	T_4	T_4	T_4	0
1×	772	L	++	++	+	0
2×	343	0		++	++	++
3×	556	+	++	0	0	0
5×	123	0	++	0	0	0
6×	575	+	+	+?	++	++
7×	161	+	++	+?	++	++
Virulence test of R1. First passage from guinea pig						
8×	584	++	++	++	++	++
9×	11		(septic infection)			
10×	352	+?	++	++	++	
11×	265		(chronic pneumonia)			
				Tracheo-Bronch.		
12×	90	–	HT_1	HT_2	0	–
13×	90	L, A_2	0	T_2	0	–
14×	90	L, A_3	T_4	HT_4	0	–
15×	191	L, A_3	T_2	0	0	–
16×	69	–	0	–	0	–
17×	126	L, A_3	T_4	HT_2	T_3	T_2
18×	100	L, A_4	T_4	T_3	0	0

Intradermic tests with small doses of tuberculin were made on the nineteenth and forty-ninth days, and again after eighteen months, when only 4 of the 9 remaining animals reacted. The reactions were definite in the 4, yet it was decided not to repeat the test again until after reinoculation. Previous experience had shown that negative reaction did not exclude the possibility of infection being present, and positive reactions were quite as frequent with a smaller dose (0.005 to 0.01 cc.) of tuberculin than that first used (0. 02 cc.). It was desirable to avoid frequent tests as the objection had been made that tuberculin treatment was being given.

We had no better criterion for their recovery than the completely normal appearance of the animals after two years.

These 9 lusty animals, all weighing well over 900 grams, seemed to us properly to be compared with completely healed tuberculosis of the lymphatic system in human beings.

It was necessary to find animals of approximately the same age for controls to the reinfection, which was difficult as the majority were at least three years old. The reinfection was given in exactly the same way and with the same strain (R1) as in the first infection, but with a fresher culture (twenty-eight days). The suspension showed two to five bacilli and a few clumps to a field. Six blasts were given to each pig, including eight healthy controls.

TABLE 6A

Series 5. Reinfection after two years R1, killed 30 and 32 days after second infection

ANIMAL NUMBER	WEIGHTS				TUBERCULIN TESTS		
	At first infection	At second infection	One month after second infection	Gain or loss	0.005 cc. 182 days after first infection	0.010 cc. 10 days after reinfection	0.010 cc. 24 days after reinfection
2	405	910	850	−60	+?	++	++
5	320	1005	985	−20	+++	++++	++++
7	435	1095	1080	−15	+	+++	++
14	330	980	800	−180	+	+	+
15	393	770	745	−65	+?	0	+
17	325	930	885	−45	+	+++	++
20	510	1060	1025	−35	++++	++++	++++
22	430	980	995	+15	++++	++++	++++
23	395	990	915	−75	++++	++++	++++
Controls: Second inhalation							
10		785	815	+30		0	++
11		775	720	−55		0	++++
12		885	825	−60		0	+++
13		665	670	+5		0	++
14		1005	955	−50		0	++++
15		630	570	−60		0	+?
17		765	720	−45		+	+++
18		940	860	−80		0	++++

Table 6 sets forth the details of the results in each series of animals as they were chloroformed in groups of 2 reinfected and 3 control pigs, on the thirtieth, thirty-second and fortieth days. With the exception of 2 reinfected animals, the controls revealed many more lung tubercles which had progressed to caseation, while the reinfected animals showed a few noncaseous lesions.

The two pigs resembling the controls never definitely reacted to tuberculin and may have escaped primary infection (though this is doubtful), since one of them did not give prompt tuberculin response on the tenth day after the last infection.

The tuberculin reactions of the reinfected guinea pigs on the tenth day are of special note, since all but no. 15 gave marked reactions, whereas none of the controls gave any response at that time. Later, on the twenty-fourth day, all but 1 control responded. The significance of these differences will be discussed later. The microscopic examination disclosed practically no fresh tubercles in the majority of the reinoculated animals.

TABLE 6B

Series 5. Reinfection after two years R1 (moist vapor), 30 and 32 days after second infection

ANIMAL NUMBER	HISTOLOGIC EXAMINATION OF TISSUES				ADDITIONAL GROSS OBSERVATIONS		
	Lungs		Tracheo-bronchial lymph glands		Cervical lymph glands	Tracheo-bronchial lympth glands	Spleen
	First infection	Second infection	First infection	Second infection			
2	–	–	–	–	+	+	0
5	L, HT_1	0	0	T_1	+	0	0
7	L, HT_2	A_2	HT_2	0	0	0	0
14	L, HT_2	A_2	0	T_1	+	+	0
15	L, HT_2	A_3	–	–	?	+	–
17	–	–	–	–	+	+	0
20	L, 0	0	–	–	++	++	+
22	L, HT_2	0	0	T_2	?	?	+
23	L, 0	0	HT_3	0	?	?	0
Controls: second infection							
10	–	L, T_4, HT_1	–	T_3	0	0	+
11	–	L, T_3	–	T_3	+	+	+
12	–	L, T_4	–	HT_1	+	+	+?
13	–	L, T_2	–	HT_2	0	+	0
14	–	T_3	–	T_3	0	+	+
15	–	L, T_4, HT_1	–	T_2	+	+?	+?
17	–	–	–	–	–	+	–
18	–	L, HT_1	–	T_2	+	+	0

SUMMARY OF HISTOLOGIC CHANGES IN GUINEA PIGS INFECTED BY THE R1 STRAIN OF TUBERCLE BACILLUS

1. *Sequence of events following the first inhalation:*

Lungs: By far the greater number of the first tubercles appear immediately beneath the pleura, where the reaction is initiated by a swelling, proliferation and desquamation of the alveolar epithelium. Within the lumen of the air sacs there very quickly appears a collection of mononuclear cells derived from various sources. Normally a few such cells appear after birth within the alveoli, which act as scavengers for the small amounts of the foreign material finding its way into the terminal air passages under ordinary conditions of life. These cells are capable of undergoing division locally to meet any increased demand for phagocytes. In addition to these, mitotic figures are seen within the lumen of the capillaries of the wall in the region of the tubercle formation; these division figures are probably within the endothelial lining. After proliferation the daughter cells pass through the vessel wall into the air space and there take part in tubercle formation. Frequent division figures also occur within the lumen of perivascular lymphatics. Long continued search of many sections has failed to detect tubercle bacilli within any of these cells, but the presence of so many division figures suggests that the cells which first respond to the presence of the tubercle bacillus within the alveoli are phagocytes normally present within the lumen, cells derived from the local blood vascular endothelium and possibly those from the lymph vascular endothelium. The reaction on the part of the epithelium is likewise a response to irritation, but these cells desquamate and soon die without taking active part in tubercle formation.

By fusion, and as a result of direct division, the remaining intraälveolar cells tend to form large, crescent shaped, multinucleated cell plaques which have very deeply stained cytoplasm. Repeated division within the intraälveolar masses fills the lumina of groups of alveoli and as a result a rather sharply circumscribed nodule, spherical in cross section, is formed (see fig. 2). The completion of this stage requires about two weeks, although the rapidity of the reaction depends upon the number of bacilli originally lodged at the point of formation.

At the same time the alveolar walls are becoming thickened, both because of the accumulation of cells within the capillary lumen which are continually passing through their walls, and also because of a moderate proliferation of the connective tissue framework in the alveolar wall. The nodule gradually assumes a more homogeneous appearance, in which alveolar outlines cannot be detected without special stains for connective or elastic tissues. The connective tissue cells lay down more and more an intercellular substance (collagen), and their nuclei become compressed. A rare tubercle bacillus can be detected by the Ziehl-Neelsen stain. At the periphery of the tubercle are alveoli which show changes similar to those already described, connective tissue thickening of the walls, and crescent shaped polynuclear masses within the lumen.

Caseation begins at the center of the mass during the third and fourth weeks and may spread outward to involve about half of the whole area. Unless the infecting dose be very large the process usually stops at this point and resorption commences (see fig. 3).

It is peculiar to this strain of tubercle bacillus—and possibly to other strains which have been long under artificial cultivation—that they can produce a caseous reaction but that instead of the process spreading from the initial foci, it slowly undergoes retrogressive changes and may finally completely disappear. Resorption is initiated by a change in the caseous material which becomes dry and granular, and may be invaded by mononuclear leucocytes. In fixed sections it appears to have shrunken away from the surrounding connective tissue. As the caseous

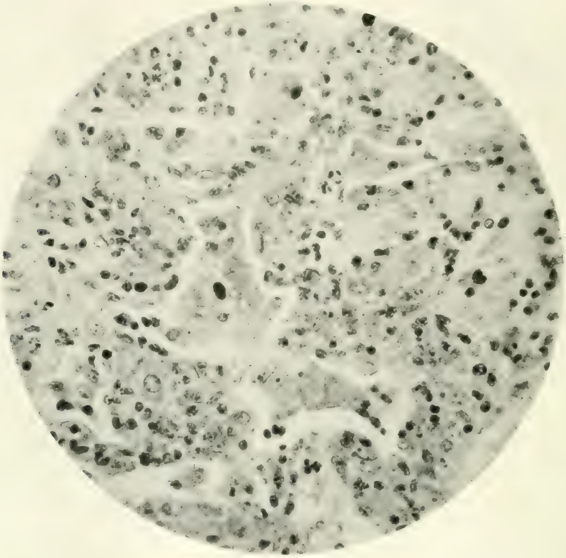

FIG. 2. HIGH POWER DETAIL OF PRIMARY INHALATION TUBERCLE

Normal outlines of lung structure obscured by proliferated cell masses.

matter shrinks it is replaced by ingrowth of this connective tissue. A definite zone of lymphocytes and plasma cells is formed, not at the extreme periphery of the mass as is usually described in tubercle formation, but along the inner margin of connective tissue next to the caseation. In the outer zone the intracellular substance contracts, leaving a structure no longer homogeneous but composed of loose strands of connective tissue with shrunken nuclei. As a result of this contraction the more or

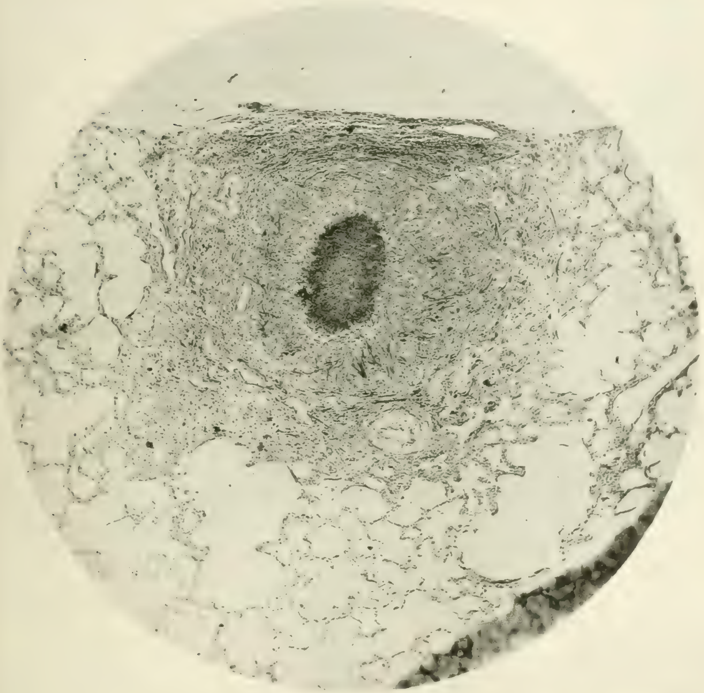

FIG. 3. PRIMARY INHALATION R1 TUBERCLE

(Aniline blue connective tissue stain.) Discrete nodule with well developed caseation and "pleural cap." Note indentation of the line of the original pleural surface.

less intact alveoli, lined by cuboidal epithelium at the periphery, are pulled inward and assume very irregular shapes. Soon they extend to the receding central caseous margin and finally, as this disappears, they come to occupy the whole area. At the height of its activity thin-walled dilated capillaries are a rather prominent feature in the young connective tissue about the periphery of the tubercle. These persist during the process of replacement of caseous matter and may become very much dilated. The final outcome is a complete resorption of all inflammatory and degenerative elements with a gradual readjustment of space relations, so that the irregularly dilated air sacs assume normal shapes and size. Numerous sections selected by a hand lens from the lungs of animals killed two years after infection have very frequently failed to show any trace of the previous lesions. The time required for the completion of the process is variable, sometimes three or four months, sometimes a year or two, and this is probably due to the difficulty of controlling the number of bacilli which are to reach a given area of the lung. But repeated examination of large numbers of animals has established the course of the process.

The pleura shares in the reaction attendant upon the growth of tubercles lying immediately beneath it. This pleural response consists in the formation of a cap of granulation tissue immediately overlying the pulmonary lesion (see fig. 3). The cap may persist indefinitely and frequently its shrunken remains serve to call attention to almost healed underlying pulmonary tubercle which would otherwise escape detection.

Shortly after the subpleural tubercles have reached the height of the degenerative stage (about three or four weeks) there appears a second generation of lesions in the depth of the lung, usually in the outer half. The lung is now sensitized by the subpleural reactions and the deep lesions, in consequence of the existing allergy, are most frequently abortive and do not tend to caseate. In this respect they resemble the reactions of reinfection to be considered below. Some few large caseous tubercles are occasionally found in this zone of the lung, but it is probable that they are of the same generation as the subpleural lesions, as they are of the same size and are usually in the same stage of advancement.

In addition to these specific changes hyperplasia of the small peripheral collections of lymphoid tissue should be mentioned. In the normal guinea pig lung there are extremely minute collections of lymphoid tissue situated at the peripheral end of the ductuli alveolares. These collections are located at the entrance of the lymphatic system. Under the stimulation of a great amount of foreign irritant which must be removed from the air passage by the lymphatic system, these masses become greatly increased in size. This is accomplished by local proliferation of their essential cells, the lymphoblasts. Such a reaction occurs in response to the inhalation of large quantities of mineral dusts or of a much smaller quantity of tubercle bacilli. In the latter case hyperplasia commences in the early stages of tubercle formation and persists long after all other traces of tubercle have disappeared from the lung. It is an important change as these large masses, frequently very numerous, are often the only trace of a previous infection which has otherwise healed (see fig. 4). Tubercle bacilli have never been observed within these masses, and it does not seem probable that the formation of specific

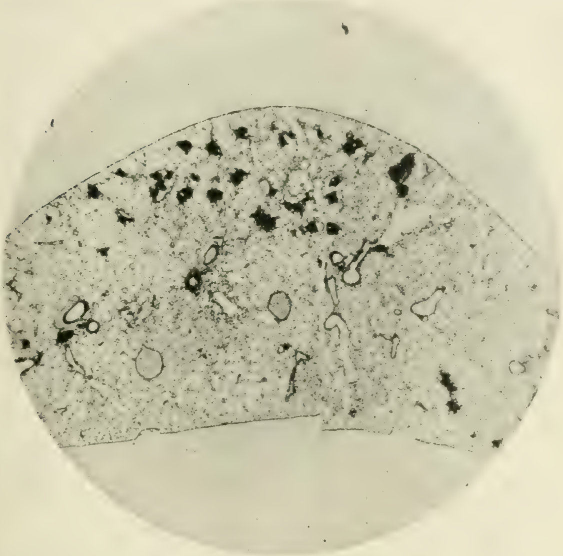

Fig. 4. Lymphoid Hyperplasia x5

No other trace of primary infection

tuberculous lesions occurs within them. It is usual to find such a mass in the immediate vicinity of a subpleural tubercle and in the later stages of resorption a definite circumscribed mass of such lymphoid cells can be found within the fibrous walls of alveoli at the site of the former tubercle.

In addition to these peripheral lymphoid collections there are those larger well marked collections located at the junction points of vessels and bronchi. These also undergo active hyperplasia with very frequent mitotic figures and a rapid increase in size. True tubercle formation *may* occur in some of these, especially those more centrally located near the hilum. Such involvement occurs if many bacilli enter the lung and are carried to these areas by the lymphatics.

To recapitulate the pulmonary changes: A primary generation of tubercles appears beneath the pleura. These progress to caseation, which is usually complete in the third or fourth week. The process of resorption which requires a variable length of time, from three months to over a year, is accomplished by the organization of the granulation tissue about the periphery of the tubercle, the gradual removal of the caseous matter, and the final absorption of the whole focus. Distorted alveoli are pulled in from the periphery and finally there remains a cluster of alveoli with thickened walls. Due to readjustment of the alveoli about the site of the former lesion the air spaces in the involved area again become normal in size and shape and all trace of the specific lesion is lost. In addition there is the nonspecific reaction of peripheral lymphoid hyperplasia which persists indefinitely and which is of great importance, as it may be the only trace of previous infection.

The tracheobronchial lymph nodes become involved with proliferative tubercle within three weeks after infection. These lesions progress to caseation and then undergo fibrosis, in which condition they may persist for a long time and then be absorbed as in the lungs. The only trace of such a lesion is perhaps a moderate distortion of structure, the compression and obliteration of some sinuses and dilatation of others. The lymphocytes of the pulp are frequently replaced by reticuloendothelial cells. The progress of resorption is irregular; it may be complete within eighteen months or it may persist longer.

2. *Sequence of events following reinfection by inhalation.*

Lungs: The early changes occurring during the first month have not as yet been studied but in all probability they are identical with those occurring in the formation of the deep tubercles of the second generation in the lungs of animals receiving only a first infection. These reactions consist in the accumulation of cell plaques and isolated mononuclear cells within the alveoli immediately about a ductulus alveolaris. This, except for the location of the lesion, does not differ from the initial reaction of a primary infection; but there is in addition another feature of the reaction, exudation manifested by accumulations of polymorphs, often of the eosinophilic type and perhaps fibrin. The nodule thus formed does not have the regular outlines of a tubercle resulting from primary inoculation; nor has it the usual compact, almost homogeneous structure. The outlines of the alveolar walls are still discernible and the masses of proliferative cells are broken up by the cells of exudation, that is, polymorphonuclears (see fig. 6). It is extremely rare for any caseation to occur but when it does there is usually necrosis of only a limited number of cells. In the great majority of cases the reaction ceases to progress and resorption commences before caseation occurs. The intraälveolar exudate and proliferated cells disappear, leaving only a moderate thickening of the alveolar walls in a circumscribed focus, which persists as such for an indefinite period. It is evident that the allergic reactions initiated in the guinea pig's lung by the inhalation of

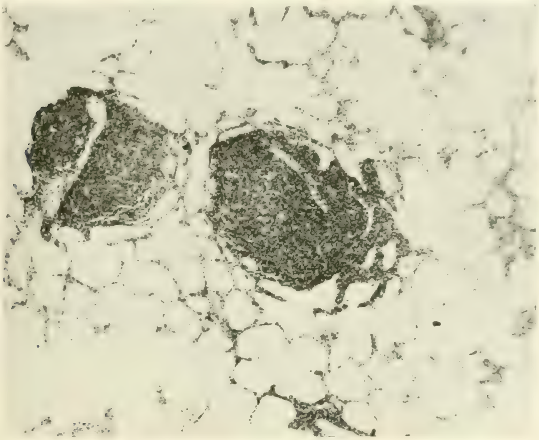

FIG. 5. DETAIL OF LYMPHOID HYPERPLASIA

small doses of the R1 strain are manifested by a very moderate, localized inflammation accompanied by atypical and abortive tubercle formation (see figs. 7, 8 and 9). The reaction remains localized, does not tend to spread within the lung, and the focus practically never caseates.

Reinfection produces no change in the peripheral lymphoid masses already hyperplastic from a previous infection. There is no evidence of a second increase in size, nor is a fresh proliferation of the cells stimulated by reinfection (see fig. 5).

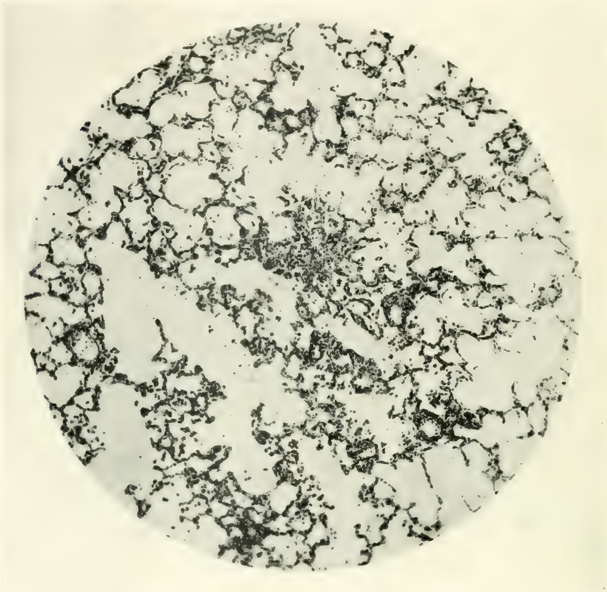

Fig. 6. Repeated Inhalation Infection, Low Power

Diffuse inflammatory reaction within alveoli; no proliferation.

The tracheobronchial lymph nodes: These nodes have been observed over a period of seventeen months after secondary infection. If sufficient time has elapsed between exposures, the primary infection may have disappeared and can be detected with the greatest difficulty. The second infection is manifested by simple proliferation which is usually very slight, often only a few cells located in the medulla or between the germinal centres. Caseation never occurs and little or no fibrosis has been observed. These few proliferated cells are probably removed by phagocytes after the bacilli are destroyed.

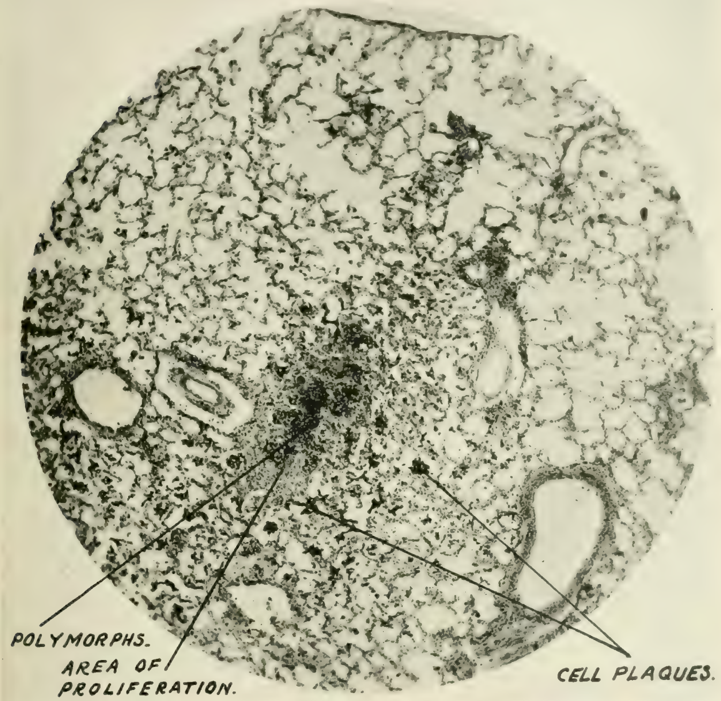

FIG. 7. REPEATED INHALATION INFECTION

Diffuse inflammatory reaction with early proliferative nodule formation. The very dark mass at the centre is not caseation but a large collection of polymorphonuclear leucocytes. The irregularly elongated masses within the alveoli are cell plaques invaded by eosinophiles.

COMPARATIVE OBSERVATIONS ON PULMONARY TUBERCLES PRODUCED BY SUBCUTANEOUS INOCULATIONS IN THE GROIN

Repeated observations by many experimenters in this and other laboratories have demonstrated the fact that the R1 strain of tubercle bacilli when inoculated into the subcutaneous tissue of a guinea pig's groin in moderate dose produces a nonprogressive lesion which heals in

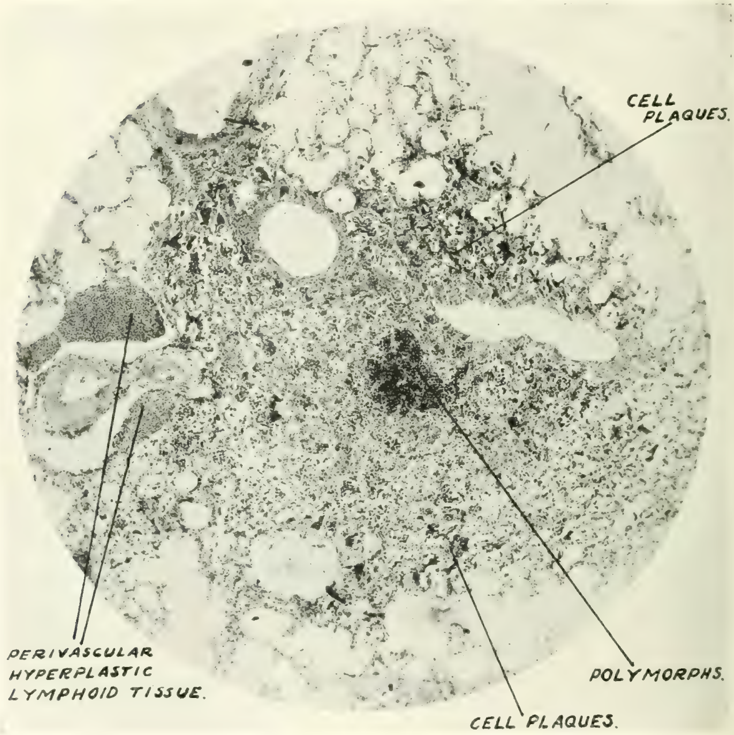

FIG. 8. REPEATED INHALATION INFECTION

Nodule formation more pronounced. The alveolar outlines are still discernible; the proliferated cell masses are interrupted by collections of polymorphonuclear leucocytes and the periphery are cell plaques invaded by eosinophiles. About the large vessel at the extreme left is a hyperplastic lymphoid mass.

all the organs except the lymphatic system. There it may remain in a dormant encapsulated condition for an indefinite period. The published results of these experiments have all been based on gross observations, however, so that it seems desirable to note briefly the sequence of events as seen in microscopic sections.

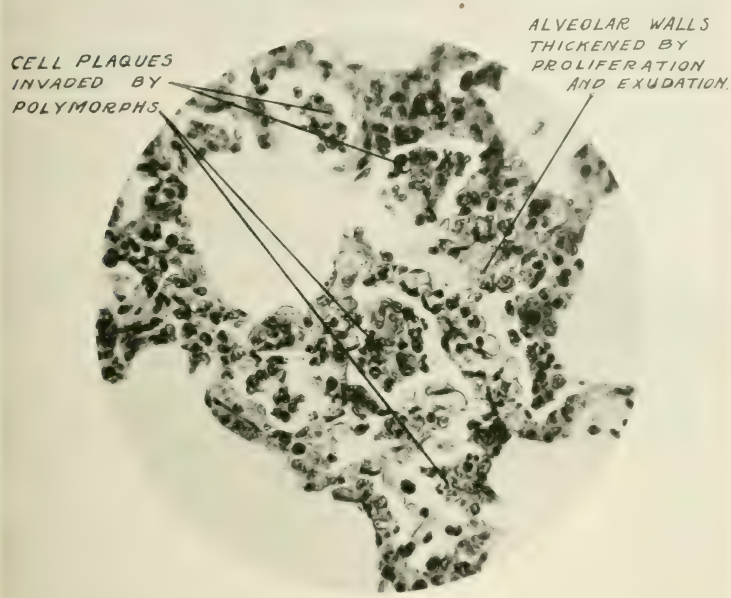

Fig. 9. Repeated Inhalation Infection

Detail of figure 6. Inflammatory reactions showing thickening alveolar walls. The alveoli contain cell plaques which are invaded by polymorphonuclear leucocytes.

In the course of another experiment it became desirable to know whether organisms of this strain when introduced subcutaneously into a guinea pig's groin could be detected within the animal's lung at varying intervals after infection. Experience had indicated that macroscopic involvement of the lung does not usually occur when small doses of bacilli are introduced by this route, but Krause has clearly demonsrated that they must pass through the lung by way of the lymphatic and venous circulation. As a control to this other experiment the work of Krause (76) was repeated in a somewhat modified form on a small group of seven animals.

The guinea pigs were inoculated subcutaneously in the groin with 0.5 cc. of a suspension of a three week's glycerine broth culture of the R1 strain of bacilli, so prepared that there were from three to five single bacilli to an oil immersion field. The animals were killed at intervals of five, twelve, eighteen, twenty-eight, thirty-nine, ninety-three and two hundred nineteen days after inoculation. The thorax was opened under strict asepsis; the left lung was tied by a double ligature at the hilum about the vessels and bronchi; section with a fresh knife between the ligatures allowed the lung to be removed to a sterile container. The right lung together with the tracheobronchial lymph nodes, was preserved for histologic examination. The left lung was then ground in a sterile mortar with physiologic saline solution and the entire quantity, usually from 3 to 5 cc. exclusive of the connective tissue framework, was inoculated subcutaneously, one-half into each groin of a second pig. Animals of the second series were killed at intervals varying from three to six months, when gross and microscopic observations were noted.

The animals of the original series showed a regular progression of lesion through the lymphatic system and spleen, as Krause has already noted. As might be expected, the general allergic state already established by a focus of disease in the inguinal lymph nodes becomes manifest in the reaction to those tubercle bacilli reaching the lungs and other viscera. As the number of bacilli reaching a given point within the lungs at any one time is so small, it is possible to study the sequence of the reaction step by step. The response consists of a localized inflammatory exudation of polymorphonuclears, fibrin, and a moderate number of mononuclear cells, probably derived from the vascular endothelium. There is also a proliferation of the lining alveolar epithelium which however desquamates, dies and takes no other part in the reaction. The amount of proliferation of fixed tissue cells varies in different animals;

in some a rather irregular tubercle-like nodule forms and in other cases a few giant cells of the Langhans type are seen, but usually there are only small scattered masses of proliferated cells which are separated by areas of inflammatory exudate. Caseation was seen in only two animals and was extremely limited in amount. The lesions are generally localized about small vessels. Lymphoid hyperplasia occurs as in the inhalation infections. Tubercle bacilli could not be detected in stained sections after long continued search.

Reinoculation into pigs of the second series, however, demonstrated that as early as the fifth day the lungs did contain tubercle bacilli capable of producing infection and that these bacilli continued to be present in such a state for two hundred and nineteen days after infection. In only one instance (thirty-nine days) did inoculation fail to demonstrate living bacilli in the lung of the animal of the first series. A larger series of animals would probably have shown that this failure was due to faulty technique, as it seems unlikely that there should be a period when no bacilli would be present in lesions which in no way differed from those preceding or following them.

As the purpose of inoculation was merely the detection of viable bacilli the animals were not killed at any stated interval after infection. There was no evidence of an increase in virulence shown in the second series, the lesions in general corresponding with those seen in the original series.

The tracheobronchial lymph nodes in both series were usually involved only with proliferative tubercle. Two animals of the original series, those of the thirty-ninth and ninety-third days, showed relatively small amounts of caseation in the centre of large masses of proliferative lesion. This might be explained by the large number of bacilli which had accumulated at that point. The lymph node lesions of the second series were all in various stages of healing.

In conclusion it may be stated that the establishment of the primary focus in the inguinal lymph nodes has sensitized the whole body. This tissue sensitization is manifested as early as the fifth day by the type of reaction in the lungs to those bacilli carried there by the lymph and blood currents. The reaction consists of inflammation which largely overshadows any proliferative phenomena; caseation is negligible and only in rare instances when large numbers of bacilli happened to have reached a given focus. The failure to detect tubercle bacilli in stained sections may be explained as being the result of bacteriolysis occurring in the inflammatory tissue, and possibly there is a change in the tinctorial properties of the bacilli. But that they are present in a viable state has been established by reinoculation. There is no evidence of any exaltation of virulence by a single animal passage.

In view of the fact that the employment of small doses of this strain of tubercle bacilli so readily allows a study of the details of development, it is instructive to compare the primary type of reaction induced by inhalation with those secondary allergic reactions produced by tubercle bacilli spreading into a sensitized organ like the lung. Without considering time relations, the lesions may be summarized as follows:

The primary inhalation lesion is characterized by the formation of tubercles appearing first beneath the pleura, while the tubercle of autogenous metastatic reinfection may appear at any point in the lung. The former are distributed by the air passages, and the latter by way of the blood vessels. Inhalation tubercles are formed by a proliferation of the fixed body cells which produce a nodule. This undergoes caseation and then heals by absorption. Autogenous reinfection by spread into the sensitized lung manifests itself as an inflammation which is accompanied by a moderate degree of proliferation on the part of the fixed tissues. Caseation with the doses here employed is very rare. What may be the ultimate outcome is not yet certain. Some of these lesions are abortive and rapidly disappear with little or no proliferation; others have persisted as long as six months and at that time are apparently in full vigor.

When compared with the lesions produced by repeated inhalations, these autogenous reinfections present a more vigorous inflammatory response resulting in larger tubercles which persist longer. Probably the question of dosage is the explanation of this difference, inasmuch as the *later inhalations* were of larger amounts.

Reference should be made to the pneumonic lesions so frequently encountered in these animals, as they might be confused with the pneumonic inflammatory reaction of the allergic lung. The distribution of this nontuberculous pneumonia is characteristic; usually it is confined to the peripheral portions of the cephalic lobes and to the central portion of the median lobe. Most of the cases from which cultures have been made have yielded a pneumococcus and in rare instances B. bronchosepticus. Repeated attempts to demonstrate tubercle bacilli both in smears and sections have failed.

Histologically the process resembles that of the organization which sometimes follows an unresolved lobar pneumonia in human beings. The bronchi are filled with serum and polymorphonuclears; the alveoli contain large numbers of monoculear cells, polymorphonuclears and fibrin. The latter frequently extends through pores into adjacent alveoli. Peripheral to this may be zones of edema, congestion and perhaps hemorrhage. With the progress of the disease the fibrin becomes organized by the outgrowth of fibroblasts along the fibrin loops, so that each alveolus is filled with a loop of connective tissue. At the same time the alveolar walls are thickened and ultimately they may be transformed into a mass of connective tissue in which are irregular air spaces lined with cuboidal epithelium. The hyperplasia of peripheral lymphoid tissue does *not* occur as a result of this type of infection; but a preëxisting hyperplasia, the result of a previously established pulmonary tuberculosis, is not destroyed by a subsequent pneumonia of this origin. It seems probable that recovery from this type of infection may occasionally occur if the process has not been too extensive. At the tip of a cephalic lobe one rarely finds all the alveoli lined with cuboidal epithelium and resembling collecting tubules in the kidney. Such healed lesions have been regarded as the final stage of a chronic organizing pneumonia, but the intermediate steps in the healing process have not been observed.

SUMMARY OF EXPERIMENTS

Series 1. Reinfection of tuberculous guinea pigs with virulent human tubercle bacilli, after eleven and twelve months of arrested disease in the lungs and regional lymphatic nodes, produced a slower and less extensive disease than in the controls. This was confirmed by *secondary* subcutaneous inoculations of the old and recent tuberculous lung tissue and by microscopic study. Heavier dosage for primary infection after reinfection eleven and twelve months later with virulent bacilli gave a contrast in the pulmonary lesions but otherwise less difference when compared with the controls, doubtless because of extensive primary infection.

Series 2, Experiment 356 (*a*). A strong primary infection followed in eighteen months by reinfection with the same culture failed perceptibly to increase the amount of disease in the lungs and glands.

Series 3, Experiment 356 (*b*). Three successive infections with R1 culture produced definite pulmonary and lymphatic tuberculosis with evidence of fibrosis. The lesions were not as numerous as those in the control animals which had received the single infection at the time the second and third inoculations were given. A definite increase of lymphoid tissue was noted in the lung periphery, corresponding to the more frequent and well resisted infections.

A control test of the virulence of R1 culture, by subcutaneous inoculations, produced chronic generalized disease in 3 of 5 animals; but larger doses were used, and it is not probable that the culture was mixed or increased in virulence.

The passage inoculations from one pig in this series were evidently virulent, and it is probable that the animal was misplaced from another cage.

Series 4, Experiment 356 (*c*). This series was not reinoculated, but was exposed to granite dust inhalation with the result that after eighteen months healed tubercles were more prominent in the dusted animals than in the controls; but the dust had not spread the disease.

Series 5, Experiment 356 (*d*). Reinfection with R1 culture after two years of arrested disease was apparently well resisted by the majority of the animals, as compared with the controls. The long interval is regarded as satisfactory proof of healed infection.

SIGNIFICANCE OF THE TUBERCULIN TEST BEFORE AND AFTER REINFECTION

The intradermic test has been considered a useful aid in determining the presence of tuberculous infection as distinguished from tuberculous disease. If given in full doses, from 0.005 cc. to 0.02 cc., in human or animal practice we expect some response, however slight the infection may have been. This is not invariably true, and our experimental work shows this fact; just as in observations on adult human beings some individuals are found not to react, although harboring old infections.

In our first two series five tests were made at wide intervals,—sufficient, we thought, to avoid the possibility of a loss of tuberculin sensitiveness due to repetition. The majority of the surviving animals reacted but once or twice after the first infection, and not so markedly after the second as the controls.

They were not tested until forty-one to fifty-five days after the second infection, when all would be expected to show new infection. The allergic reaction after subcutaneous infection usually develops within eight to ten days, but with inhalation we found it required from twenty to forty days after primary infection to elicit a reaction. This was seen in our fourth series, where none of the animals responded to a primary low virulent infection on the seventeenth day.

The phenomenon is quite different after reinfection as seen in series 3, where nineteen days after the second infection a sharp reaction followed the smallest dose used (0.005 cc.).

The most significant indication of the differences is given in the last series, table 6, where the controls gave no reaction on the tenth day following the infection, whereas the long arrested, reinfected animals promptly reacted.

We can conclude that the latent allergic power was reactivated by the new infection; and that, except in occasional animals that escaped with little or no primary infection, the power to resist was present despite the absence of a tuberculin reaction to reveal it. Doubtless a subcutaneous test would have caused a reaction at any time after the primary infection, as in human beings,—provided a sufficiently large dose is used. There are individuals who have very slight skin sensitiveness, and in whom even subcutaneous injections fail to arouse reactions within the limits of maximum dosage as usually given. It cannot be safely inferred, however, that these persons or animals have never been infected.

This is notably true of tuberculous cattle. It is generally assumed that a negative result of tuberculin tests in hdalthy subjects indicates one of two possibilities: that the individual has never been infected (chiefly true of children), or that the lesion is completely encapsulated and obsolete. We must also reckon on the incubation period of a recent infection, and we have seen that it can be shortened in reinfection, when the formation of tubercles is hastened.

PHENOMENA OF REINFECTION

The question is naturally brought up: Can the tissue cells ever completely lose their ability to react more vigorously to the presence of tubercle bacilli after having once formed tubercles?

We believe it doubtful. The experience of von Pirquet (80), Löwenstein (81) and our own experiments with the conjunctival tuberculin tests (Baldwin (82)) point to the latency of sensitiveness. A tardy or negative result from tuberculin applied to the skin or eye may be changed in a few days to a marked reaction on repetition of the same dose or less. In these experiments where an interval of nine months to two years has elapsed between successive infections, we have further evidence of prolonged latency of sensitization.

Much the same phenomenon obtains, we may believe, in human reinfection, the pathologic changes ranging all the way from a small transient collection of cells to acute pulmonary or lymphatic infiltrations and pneumonias. The latter may be entirely absorbed, or leave behind chronic disease.

The whole course of chronic tuberculosis from its inception throughout is inevitably influenced by these reactions. Von Ranke (83) has made a classification of tuberculosis on the basis of these successive metastatic changes. The underlying nature of sensitization is a field not to be entered here, but the changed reactions in tuberculosis are clearly due to intracellular qualities dormant for long periods.

AUTOGENOUS OR EXOGENOUS REINFECTION

Our experiments are, we believe, to be interpreted as solely exogenous reinfections, and so far as they show anything as to the possibility of natural reinfection in the animals they indicate clearly enough that it may occur when relatively large doses are given by inhalation. Primary intestinal infection as evidenced by mesenteric gland involvement was exceedingly rare in our animals, and the inference is justified that it played little or no part in the reinfection. The submental and cervical glands were occasionally found to be tuberculous from the primary infection, suggesting the simultaneous entry of the bacilli through the nasopharynx and trachea. The majority of the foci were found subpleural in the lung periphery, where, according to the anatomy of the parts, foreign particles deeply inhaled are likely to be held. It is the region where the bronchial cilia are absent and the lymph stream in the human lung communicates with the pleural lymphatics (Miller (84)) and thence into the interlobular lymph channels toward the hilum glands.

From the pathologic study we found both primary infections and reinfections followed the above order, but with a difference.

The second infection did not form the caseated tubercles with the regularity seen in the primary tuberculosis; instead, a localized inflammatory reaction with a moderate degree of proliferation without caseation was the rule. The tracheobronchial glands suffered no further disease in the mild reinfections; in short, an abortive form of the disease followed, with some exceptions which can be explained either by overdosage or by absence of primary infection.

We wish to acknowledge the valuable assistance in the course of the experimental work of Miss Hildegard G. Henderson and Mr. Richardson Murphy.

PART II: REINFECTION IN ITS CLINICAL AND EPIDEMIOLOGICAL ASPECTS

Can we translate the knowledge of reinfection phenomena obtained in animals into terms of human tuberculosis? This has already been done to such an extent that some investigators and writers pronounce the belief that all tuberculosis orginates in childhood from primary infection which later spreads in the body.

To assert this with confidence would be to ignore clinical facts; but to ignore the evidence of immunity would be equally narrow.

It is with no feeling that a final statement can be made that we venture to bring together the evidence as to the origin of clinical tuberculosis. A full consideration of primary infection, its sources, virulence and amount, manner of entrance into the body, and its progress or arrestment, is needed to fully understand the ultimate issue. There are, besides, the factors of race, heredity, structure, disease, nutrition, environment, and a host of minor influences to bring into line. We shall limit ourselves to a few points in this essay. So far as animal experiments with the use of culture bacilli can hold, we must recognize some limitations in interpretation and not be too literal in applying the results. There is at present, growing out of the great war, an enormous clinical material available for studying the subject of infection. The chapter of pandemic influenza is also not yet closed as to its effect on tuberculosis. There are many recent contributions on all these subjects, and the epidemiology of tuberculosis is also being rewritten in the light of forty years of accumulated observations on infection.

PRIMARY INFECTION AND ITS RELATION TO AUTOGENOUS REINFECTION

It can be of little importance here to present the arguments for and against the different ways by which the bacilli of tuberculosis can get into the body. It will be granted that most primary infections enter by the respiratory or digestive tracts. Doubtless there are some directly inoculated either into the skin or mucous membranes by slight abrasions, or even through the conjunctiva (Corper (85)). But by whatever channel, the lymph nodes sooner or later receive and harbor the bacilli, whether of human or bovine origin. It is even admissible that a few instances have been derived from avian sources (Koch and Rabinowitsch (86)).

All experimental evidence points to the respiratory tract as the most important avenue of infection, except where bovine infection in children is unusually prevalent, as in Scotland and England (Griffith (87)). It is reasonable to hold this view, inasmuch as inhaled bacilli are capable of infection in such small numbers as compared with ingested bacilli (Findel (88), Reichenbach (89), and Selter (90)). These statements do not minimize the importance of infection by way of the upper air passages and mouth.

Frequent inhalations and repeated ingestions are readily conceivable in badly infected surroundings, so one need not dogmatize on that phase of the subject, since the result is the same and simultaneous infection through several channels is probable.

There has been much controversy also over the question of tubercle bacilli dormant in the tissues, without the formation of tubercles, especially in the lymph glands.

The extensive work of Harbitz (91) showed that, in 18 out of 91 children, inoculations proved the presence of bacilli, most often in the cervical lymph nodes without microscopic lesions present in the latter. These, were mostly in children under one year of age (10 of the 18). He believed that the bacilli might rest three to four months in the nodes. Macfadyen and MacConkey (92) inoculated mesenteric node tissue of 20 nontuberculous children, with 5 positive infections. Rosenberger (93) also found latent bacilli in 6 out of 14 cases, both adults and children, who were nontuberculous. Goodale (94) reported 3 positive inoculations in 8 tonsils which showed no tubercles. Bartel (95) has contributed much to the subject of lymphoid tissue pathology in tuberculosis, and holds that the bacilli are weakened in virulence by residence in the nodes, often remaining three or four months with no tubercle formation.

Hamburger (96) noted the time of development of tuberculin susceptibility in children after exposure to infection and found that it came on very slowly, as in inhalation or feeding animal experiments. In 3 of 15 cases in children Wolff (97) claims to have found Much granules in the mesenteric lymph nodes, which seemed otherwise normal but which were positive for tuberculosis by inoculation.

A number of observations on cattle have been made which show the presence of bacilli with absence of lesions (Rievel (98), Linnenbrink (99)). Joest (100) and Jonske (101), however, in bovine lymph tissue always found tubercles present when inoculations proved positive.

The inference is fair that in primary infection, at least, tubercle bacilli may be carried slowly into deep seated lymph nodes and remain for a time without creating a cellular reaction. Whether they can multiply without causing some response is not certain, but the numbers found in non-tuberculous nodes are always few. During the supposedly dormant period the fate of the infection is decided for or against disease, however slight this may prove to be. In the event that the tissues are able to repel the bacilli, a lymphoid hyperplasia may follow without further lesion or evidence of tuberculosis, according to Bartel (95).

We need not here consider the cases of manifest, progressive disease but only those which develop small primary foci in the lymph nodes. These probably cause few or no symptoms, and in a brief or longer period disappear, become fibrous or calcified.

Since our study relates to healed or arrested tuberculosis, these primary foci, mostly found in the cervical, tracheobronchial and mesenteric nodes, are of special interest in their bearings on reinfection.

Küss (102), H. Albrecht (103) and Ghon (104) are the principal authors who have made a careful search for primary lung foci in children and their studies have brought complete confirmation of the so called "law of Parrot." This law is in effect that tuberculosis of the tracheobronchial nodes is always accompanied by a focus in the lung, and vice versa.

It is to Küss that we are indebted for the first clear cut conceptions of inhalation infection in children, in whom we must look for the earliest evidence of infection. He found, as in experimental inhalation, that the primary focus was usually subpleural and the chain of bronchial lymph nodes became involved in succession toward the hilum and with increasing intensity as the disease progressed. Caseation of both the original focus and the lymph nodes is the rule in primary infections, which, if completely arrested without softening and ulceration, become fibrous and calcified in time. The primary focus in the lung is sometimes too small for recognition in gross sections; and no doubt there are instances of entrance of the bacilli into the lung parenchyma without persisting traces of anatomic change. For an exhaustive study of this subject the reader is referred to the monograph by Ghon, who also reviews the work of Küss and others (105).

For our purposes a consideration of these primary infections in the lung, as the most common source of old calcified and fibrous tuberculosis of the bronchial and mediastinal group of lymph nodes, appears justified. Pulmonary tuberculosis in the adult can no doubt be connected causatively with other than inhalation infection, yet reëntrance of the bacilli by other channels cannot be of frequent occurrence in the classic type of apical tuberculosis when no signs of involvement of regional nodes are found elsewhere. Primary lung foci have been demonstrated in adults in a few cases; Ghon and Pototsching (106) cite four such cases recently, but they are rare in Europe, and resemble the usual childhood type in their progress and involvement of the tracheobronchial nodes. As to the frequency of the primary lesion in the lung as compared with the other pathways, Ghon's figures are impressive: In 185 cases, 162 or 88.05 per cent were traced to the lung; in 155 of these the primary focus was demonstrated by microscopic examination. One case was traced to the tonsil, 3 to the intestine (ileus), 1 to the skin, and 15 to another organ simultaneously with the lung, 13 of which were in the intestine. In 2 the focus could not be traced. Canti (107) looked for primary lesions in autopsies on children up to ten years of age. He found 16, or 19 per cent, showed tuberculous lesions, confirming Gohn's description.

CALCIFIED REMAINS OF FORMER TUBERCULOUS FOCI

Pathologists have been accustomed to regard the completely fibrous and calcified tubercles, found frequently in otherwise nontuberculous subjects, as incapable of causing new foci. There are exceptional instances of ulceration into the wall of a vein, but these are often only partly calcified tubercles and contain caseous or purulent material.

The completely obsolete tubercle is not, as a rule, uniformly infectious for guinea pigs, but even this delicate reagent may fail when a few living but feeble bacilli are inoculated. The study of these remains of first infections has been revived in recent years, particularly since the discovery by roentgenography of their enormous frequency at all ages. Lydia Rabinowitsch (108) has given much attention to the virulence and types of bacilli in the encapsulated old tubercles. In 44 per cent of 34 calcified glands she obtained positive inoculations. She also found 5 atypical bovine forms in 37 cases. In a thorough review of the subject she concludes that the encysted bacilli found in subjects otherwise tuberculosis-free are no less virulent than sputum bacilli (or bovine, as the case may be).

Schmitz (109), on the contrary, found 7 of 26 calcified tubercles positive on inoculation, but of weak virulence. In support of this, he found no increase of virulence by passage from one guinea pig to another. Six of 8 chalky, soft tubercles, were also positive.

Wegelin (110) made histological examinations of 12 calcified tubercles from various lymph nodes, treating the tissue with antiformin, decalcifying and then staining. Four positive cases were demonstrated, and of 3 chalky foci all were positive. In his opinion the bacilli in such lesions would be mobilized with difficulty.

In cattle and swine calcified tubercles are found to a much greater extent and may be present even in rabbits and guinea pigs in chronic tuberculosis.

They occur at relatively young ages in calves, and the lime salts are deposited in younger tubercles than in human subjects. According to Lubarsch (111) calcareous remains of tubercles are rare before the third year of life in children. It is recognized that such lesions may be the remains of other parasites, and microscopic or inoculation tests are necessary to prove their tuberculous origin (Beitzke (112)).

Notwithstanding the absence of the last mentioned criteria, the findings in X-ray negatives are so characteristic and have been so abundantly confirmed by microscopic examination, that the great frequency of these remains of early, healed infections is now well recognized. Naturally it has always been difficult to find primary foci at the *postmortem* table, where extensive disease usually obscures all traces of early stages.

The localization of primary foci in the child is important in contrast to tuberculous disease of the adult, in that the former may occur in any part of the lung, whereas the apical tuberculosis is the predominant type after childhood.

These facts have been brought more clearly to view by the combined X-ray and pathological studies of Opie (113) in recent years. Roentgenograms of the lungs of a large number of adults and children were made after death, with remarkable revelations of first infections of the lungs and tracheobronchial nodes. These foci were very often quite extensive and in all stages of calcification. In his first study he concluded that focal tubercles identical with those of children were found in 92 per cent of all adults, which "may have been acquired between the ages of two and ten years, but in more than half of all individuals (in St. Louis, Missouri) makes its appearance between the ages of ten and eighteen years."

He also comments significantly in his summary: "Tuberculosis in children does not select the apices of the lungs, is accompanied by massive tuberculosis of regional lymphatic nodes, and exhibits the characteristics of tuberculosis in a freshly infected animal." He also finds that the lung lesions tend to heal with increasing frequency between the ages of ten and eighteen, owing to the higher percentage found between those ages.

In a later study (114) of 66 British soldiers who died in France he found 18 with caseous or calcified mesenteric lymph glands, and in the latter rarely any focal disease in the lung. The inference is plain that intestinal infection from bovine sources is more frequent in Great Britian, since no instance of healed mesenteric tuberculosis was found in 50 adults in the St. Louis study. Furthermore the absence of focal disease in the lungs when the primary infection occurred through the intestines points to the protective influence of the first infection.

The contributions of Opie are especially important because they confirm the experimental observations in several respects, and differentiate the characters of primary and secondary infections very sharply.

AUTOGENEOUS REINFECTION

The question to be decided by our study, if possible, is how often the healed tubercles just described are responsible for the successive invasion of tubercle bacilli into the other parts of the lungs or distant organs. We have learned from pathological studies that there are various degrees of healing in a caseated focus. These may range from the stage of recent caseation and fibrous encapsulation to a hard, calcified nodule or softened debris ready to break through into a vein or bronchus. We have also seen that among city dwellers at least, where large numbers of hospital autopsies are made, the percentage of healed primary tubercles steadily increases from the age of the two to eighteen, after which evidences of previous infection are practically universal among this class of people.

It seems clear that the majority of early infections after the second year, whether single, multiple, or cumulative, are mild in effect. Either quantitatively or qualitatively they are insufficient to generalize in the body; or, as some profess to believe, the glandular system in childhood is so constituted as to arrest tubercle bacilli better than in adults. There is no real basis for such a belief, so far as we know, and it may easily rest on the false interpretations of the immunophysiology involved and the amount of the infective virus present.

In point of fact, there is reason to think that successive, small exogenous infections do occur in young children, which act as preventives of severe infection up to a certain degree, or which finally break down the resistance until a chronic disease is developed. There is experimental evidence with calves to support this; and our own observations with repeated inhalation infection with low virulent bacilli tend to the same conclusion.

The pathologists have long distinguished between the pulmonary tuberculosis of childhood and adults, and volumes have been written to account for the apical disease of adults in contrast to other sites of the disease in children. The apical adult disease may have the character of a primary lesion like that in children, but does not as a rule; and disputes have long raged whether it is of aerogenous or hematogenous origin, both of which are admittedly possible.

There is also the chance that the apex may be involved in an extension from the cervical and supraclavicular lymph nodes across the pleural surfaces. There are some who believe that a back flow or retrograde current of lymph may carry bacilli from the tracheobronchial nodes into the apices as a result of obstruction from disease at the hilum. As Tendeloo (115) has shown, there are physiological reasons why the apices are more favorable both for aerogenous and hematogenous infection. The blood and lymph movement is more rapid in the bases and tends to to sweep along the foreign particles that may then lodge in the slower stream at the apex. By whatever route the bacilli gain entrance into the blood, it may be expected that the cranial portions of the lungs will be more endangered. On the other hand direct lymphogenous metastasis not infrequently spreads from the hilum glands peripherally into the lung, and we know that autogenous reinfection occasionally follows the erosion of an old focus and the aspiration of its contents, to be absorbed again from the bronchi into the interlobar lymph spaces.

What proportion of the old foci is then responsible for the clinical disease of adults?

Some years ago it was thought that the tuberculin test would tell us who was in danger of developing clinical tuberculosis. It has proved valuable in calves within limits not well defined. It is too delicate for human beings and except for young children does not distinguish clearly between recent and old infection. The positive reaction is found too frequently in adults to make any discrimination possible. The oft quoted experiment of Franz (116) with recruits for the Austrian army is an illustration of the difficulty. Of 1002 men tested in 1902 by subcutaneous injections (doses of 0.001 to 0.003) 68 per cent of those who came from localities with much tuberculosis reacted. From healthier towns, 38 per cent were positive. During the following three years 46 developed open active disease while in military service, and after another period of four years, 18 more. Of the total number, 64, who became ill in seven years, only 46 had reacted originally to tuberculin. The dose of tuberculin was doubtless often insufficient to produce a reaction; but the evidence, so far as it applies to the development of clinical disease from latent infection, was not favorable to such a theory.

The experience with the subcutaneous test at the Trudeau Sanatorium is also applicable to this question. Brown and Heise (117) report 280 reacting cases which were traced after discharge. All had a history of some symptoms but the diagnoses were uncertain, and in most cases the patients were under treatment only for short periods. After five years, 41 or 18 per cent had developed further disease, and 6 had died of tuberculosis—a very small proportion.

A study of recent literature reveals attempts to answer this question from the pathological and clinical experience in the great war. Agreement is not very noticeable except that the majority of active tuberculosis developed while in military service is ascribed to preëxisting infection, whether recent or remote. Most wounds of the lung failed to arouse old foci into activity; those instances that were recorded could be attributed to a recent or "active" latent disease (Frischbier (118), Orth (119), Bernard (120), Tecon (121)).

Trauma and excessive strain or exposure have the most important bearing on the breakdown of incompletely healed foci. Hemoptysis in hitherto healthy persons is a familiar example of the onset of metastasis from a dormant lesion, whether due to the above mentioned influences or not. Belief in the mobilizing of tubercle bacilli from a hard calcified focus has but little support, considering the great number of healthy individuals who carry them through life. We must rather look for the source of metastasis in the incompletely healed caseous foci or in those which have become softened and ruptured. Trauma and strain, as well as diseases involving the same organ, can hardly fail to endanger such foci.

It is obvious that the more recent the primary infection, the greater the danger from a partly healed focus; and, furthermore, the more virulent or the larger the dosage in the first infections the less one should speak of healed tuberculosis, however free from symptoms the individual may be. The line between healed foci and latent disease is very indistinct.

In this respect many persons infected with tuberculosis, especially children, are in the same condition of "labile infection" that a chronic malarial subject suffers (Schilling (122)), because the parasites are dormant. A long period may pass without symptoms when a relapse may occur in consequence of an intercurrent disease, exposure or overstrain.

How often do we see children enjoying good health for prolonged periods, but with intervals of febrile disturbances, short attacks of bronchitis or gastrointestinal disorders, without adequate cause?

It is a subject of increasing interest to pediatricians when these symptoms occur in children giving positive tuberculin reaction and suspicious hilum shadows in the roentgenogram. As they pass over adolescence into full maturity it should cause no surprise if a considerable number should develop autogenous metastases.

The statistics of the Trudeau Sanatorium furnish valuable evidence of autogenous reinfection covering patients of sixteen years of age and upwards. If we select only the cases discharged apparently "cured" and apparently "arrested", during thirty-five years, 45 per cent of those traced are well and 38 per cent are dead. There are 11.6 per cent classed as "living," and in 5.3 per cent their condition is unknown (vide 36th Annual Report).

The mortality from this selected class is from two to three times the expected rate, according to Brown (123), and in from 60 to 70 per cent of those who died the cause was tuberculosis.

So far as these figures apply to latent and inactive disease, they show the relapsing character of preëxisting foci. If it be maintained that new infection from outside relighted the old disease, the evidence is all against the supposition.

It is also of interest to note that ten years after discharge the mortality rate of these patients as compared with the general popluation is not as high, an indication of complete cicatrization and healing of the foci in those who did not relapse.

According to the theory of lessened tuberculin sensitiveness coinciding with greater susceptibility to reinfection, the long healed patient should again be liable to exogenous infection, yet in the above mentioned statistics there is no foundation for this belief. This "positive anergy" (von Hayek (124)) must be distinguished from the negative phase of immunity (see p. 502).

Statistics have been adduced by Ritter and Vehling (37) to connect childhood infection with adult disease, from sanatorium histories of 200 patients. There were 165 or 82.5 per cent who gave histories of positive tuberculous symptoms or strongly suspicious illnesses in youth. It was also noted that those who had early symptoms of infection were in earlier stages and in a more favorable condition. Of those with family exposure to tuberculosis in childhood, 32 per cent were in the third stage (Turban scale), whereas 43 per cent of those with no such exposure were in the same stage. The inference from the last statement is that the disease was due to recent infection and was acute from the onset.

Bruck and Steinberg (125) investigated 300 cases of tuberculosis in Breslau in as many different families where the histories were considered reliable. There were 90, or 30 per cent, charged directly to childhood infection. There were 102, or 34 per cent, without childhood exposure but with definite adult exposure, and 35, or 11.7 per cent, who lived both periods under exposure. In 73 cases, 24.3 per cent, no source could be discovered. (In passing it is worthy of mention that in these families 43 persons were found who had been fully exposed but who did not develop the disease.)

Hillenberg (126) studied 1000 cases of tuberculosis in the city of Leitz from the point of view of the time of infection. He attributed 58.6 per cent to sources of infection unknown; 26.9 per cent were in close contact with tuberculous patients. There were none of 101 cases classed as "severely infected" in childhood who lived over 40 years; hence those who lived 45 years or more he ascribed to infection later than childhood unless there was a history of family disease.

Tillisch (127) also presents the study of 841 cases, among which 168 or 20 per cent were traceable to family infection in childhood up to the twelfth year. Clinically recognizable tuberculosis was found in 107 who had no opportunity for infection at home in infancy, but 25.5 per cent of these had later exposure outside their homes. Of 156 patients there were 69 or 44 per cent who were classed in point of time as late family infections, not having had childhood exposure.

Ward (128), who studied tuberculous infection in an English rural district (South Devon) cites 316 adults over 16 years. He attributes 140, or 44.3 per cent, to immediate infection, that is, recent (?). There were 112 not traceable, and 20 doubtful.

When we review the reports of tuberculosis developed during the war it becomes more evident that little was due to fresh infections. Röpke (129) considered 90 per cent of the cases due to reactivation of latent foci. H. von Hayek (130), however, in 1917 reported on 1100 tuberculous soldiers and claims that he had seen a large number of cases in which no suspicion of previous infections could be extracted from their histories. Only 40 per cent had a family history of tuberculosis. In a later analysis of 2013 cases in 1920 the same author (131) makes the significant admission that most of those considered free from tuberculous infection before military service were the acute cases, whereas the "predisposed" patients (1633 cases) seemed better protected against severe disease. Zadek (132) and Schmid (133) confirmed these observations. L. Jacob (134) also reports 40 severe cases with only 11 manifesting suspicious symptoms in their past histories. Müller (135) considered that the army tuberculosis confirms the hematogenous theory of the extension of tuberculosis from latent foci. Less chance of infection existed, because open cases were generally kept at home.

The pathological examinations of soldiers are theoretically a better criterion of the frequency of latent tuberculosis liable to cause metastases than clinical histories.

In all the armies the haste necessary in autopsies made careful search impossible. Carl Hart (136) reported 601 men who died of wounds, accidents or acute infections. Twenty-eight were found tuberculous. Disregarding these, 196, or 34.2 per cent, of the other 573 showed signs of latent infection. Of the latter, 151 cases or 26.8 per cent appeared obsolete. From these and other considerations he does not believe childhood infection as a rule to be the source of endogenous reinfection yet there was not clear proof of any recent infection while in army service.

Beitzke (137) found five to six times more acute cases in the autopsies of soldiers in 1919 than in civilians. Twenty-nine per cent had both primary and secondary lesions, that is, caseous lymph nodes as seen in children. One-fourth of the 120 fatal acute cases with caseous glands possibly acquired the infection in the army. G. Gruber (138) found 20.8 per cent of latent tuberculosis in his army sections, many of which he thought might flare up into fresh disease.

The examinations of Opie have already been mentioned. It has been reported that other American pathologists found but few healed latent tuberculous lesions in the men dying from wounds or other diseases in the American Expeditionary Force (Webb (139)). This fact is undoubtedly to be associated with the elimination of thousands of suspected or actually tuberculous recruits during the draft or army examinations. Unfortunately there were not many autopsies in which a careful search was made for tuberculous foci, although according to Webb about 2000 were satisfactorily examined with rarely positive findings. Glomsett (140) reported 44 in 308 autopsies and later 54 cases, or only 16.6 per cent of all cases carefully searched (Bushnell (141)).

Robertson (142) found less than 25 per cent in American soldiers, but when working in Germany in 1914 he made 100 autopsies of German soldiers, including older men, and found in 70 per cent of them tuberculous deposits in lungs or bronchial nodes. Reports from the other armies are not available to us, but it is obvious that little new can be learned from them, owing to the difficulties of such research.

The main question of course hinges upon the number of tuberculous lesions that might be regarded as sources of autogenous reinfection. It was generally admitted that wounds of the chest were rarely followed by a tuberculous outbreak. Leon Bernard (120) published observations on 475 pulmonary injuries, including 379 chest wounds and 49 thoracic contusions. Only 3 of the first were complicated with tuberculosis, while 6 per cent of the latter developed the disease.

The war gas poisoning was also a negligible cause of awakening latent tuberculosis in all the armies.

The experience of Tecon (121) with interned soldiers in Switzerland is noteworthy in the same connection. Among 27 men with penetrating wounds of the chest, 5 or 18.5 per cent developed open tuberculosis. Nevertheless, among 1033 cases of lung disease treated in Leysin, 53 or 5.1 per cent had penetrating wounds of the chest; but among the latter only 1.1 per cent had open tuberculosis. Contusions were recorded in 15, of whom 7 had open disease and 2 clinically positive tuberculosis.

The opinion is therefore expressed that blows on the chest are more often exciting causes of reinfection.

The examination of 2,754,000 men between the ages of eighteen and thirty by the United States draft boards, however imperfectly done, constituted in itself a colossal statistical study of the prevalence of pulmonary tuberculosis in the United States. There were 82,000 rejections for tuberculosis, a rate of 30 per 1000. There were 55,631 frank cases recorded, and 17,119 cases of suspected tuberculosis or "weak lungs."[6] In addition there were 9312 cases of tuberculosis of other organs than the lungs (143).

A little reflection will emphasize the importance of these figures in terms of latent tuberculosis, whether due to autogenous or exogenous infection. So far as pulmonary tuberculosis was correctly diagnosed in apparently healthy men, disregarding the frank cases, one must assume that there had been a metastasis of a former infection or a new exogenous infection, in their lungs, and, according to prevailing ideas, implanting itself in the apices.

In either event the result was the same,—assuming that no symptoms were present: they were already quiescent or arrested lesions, probably many completely healed.

It was practically impossible to follow up these rejected men although an effort was made by tuberculosis associations to do so.

On the part of the Army it was to be expected that the proportion who would develop tuberculosis in an active form would be very small. This was in fact true, and except for those who broke down early in their service,—who may be regarded as latent cases previously overlooked,—the later ones may be ranged in the category of new exogenous infections. An effort was made by Webb (139) to secure evidence to support this latter view by reasoning that many young men in the American Expeditionary Forces were not previously infected and therefore received a severe primary infection while in France.

This point he supported by the death overseas of 300 men from acute forms of tuberculosis. Bushnell (141), however, combated this view on the ground of the general failure of the pathologists to search sufficiently for remains of old infections, as well as the recognized immunity to exogenous infection of the civilized white race. Acute secondary tuberculosis could also result from Army service conditions.

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[6] Among the first million men accepted by the draft boards were 14,000 who were rejected later by the special tuberculosis examiners of the army, and about 4000 were dismissed from subsequent drafts.

Downing (144) also reported 115 autopsies of men dying of tuberculosis in two Army hospitals in the United States. Half of the cases had been overseas, the remainder in various camps in this country. Only one case of acute primary tuberculosis was discovered, and this a colored man from overseas.

It must be considered that opportunities for massive infection by contact were undoubtedly present and might be considered important under service conditions in crowded quarters accompanied by filth. The real question is whether any considerable number of tuberculous soldiers were seriously infected in this way, and whether this infection was so severe or frequent as to overcome any acquired resistance which they might possess from previous infection and thus simulate the course of a primary infection. Secondly, it is to be questioned whether inhaled bacilli were responsible for many cases.

The matter can be presented another way: Is it not entirely possible in view of the disclosures made by the wholesale examinations, that the natural course and intermittent stages of progress and quiescence of an early infection finally came to an acute stage under the war strain? Inasmuch as we are obliged to depend to such an extent on statistical data of clinical material for hints of the truth, it will naturally be asked whether or not the 3 to 6 per cent (variously estimated) of any group of supposedly sound men between eighteen and thirty years of age, who are found to have some signs of pulmonary tuberculosis, can furnish the entire crop of clinical cases without acquiring additional infection from new sources.

In short, do they acquire more exogenous infection to make them actively diseased, or is it only necessary to activate what they have previously acquired?[7] Before attempting an answer, there are even better opportunities now available to decide this question.

Among these are the revelations of systematic examinations recently inaugurated in the United States, notably the Michigan Tuberculosis

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[7] According to Orth, (145), the well known Berlin pathologist, the early infections predispose to later exogenous ones, in that way explaining why early contact with bovine tubercle bacilli may pave the way for a human infection. At the same time he holds the belief that a gradual transformation is possible of the bovine into a human type of bacillus by prolonged residence in the human body. Neither view has wide acceptance, nor is either supported by direct evidence.

Survey, (146) the Framingham, Health and Tuberculosis Demonstration, (147) and the work of the Life Extension Institute. These agencies and the tuberculosis clinics have found and are bringing to light numerous inactive, closed pulmonary cases which are to be classed as potentially diseased without additional infection from outside.

In the Michigan Survey of 1915 and 1916, 11,528 persons were examined and 2914 diagnosed as positively tuberculous, 3231 as "suspicious" and 404 listed as "arrested cases" (146).

If the figures of the city of Framingham are taken as an illustration, there is an ample number of such cases to furnish the yearly mortality from tuberculosis. It has been customary in the past to estimate the number of living tuberculous persons at from 3 to 5 for each death. Counting both active and arrested cases discovered during the first two years of the survey in Framingham, a typical American city, the ratio was 21 living cases to 1 death.

At the end of 1920 the total number of "arrested cases" under observation was 120 in a population of 17,033, of whom 13,000 had had some sort of examination (148) including infants, school children, and employees in industrial establishments, and representing all ages. In the medical examination up to November, 1918, there were only 38 per cent of those examined between the ages of fifteen and forty-four, out of a total of 4473 individuals (147). The age percentages of later examinations are not yet available. The arrested cases are nearly all pulmonary and chiefly adults, and therefore the figures are more impressive in relation to the adult population.

It is to be noted that many suspected and contact cases were found but were not included in the list of "arrested cases". The total incidence of active and arrested disease for the first four years was 2.15 per cent of those examined, varying greatly with racial groups (149).

The special value of the Framingham study is that the work covers four years and is continuous. The fate of the arrested cases, of whom 50 per cent gave no history of previous symptoms, will be followed with interest, since practically all, 115, were at full time work in 1919 (150). A total of 356 tuberculous cases was brought to light, many of whom had had long histories of symptoms. The conclusion is given by Armstrong from the experience of four years that at least 16 per cent of all the discovered tuberculosis cases will be fatal (151).

INTERCURRENT DISEASES OF THE LUNGS

The influence of inflammatory affections of the lungs and bronchi has been studied with the object of determining the number of those in whom latent foci are activated. The influenza epidemic of 1918–1919 was possibly the best opportunity ever presented for these observations.

Fishberg (152), soon after the epidemic, had not seen evidence of latent tuberculosis awakened by influenza. Only 4 per cent of the arrested cases under observation at Framingham had influenza, and they not severely (Armstrong). In following up 220 cases of influenza in Buffalo which had respiratory sequelae, only 8 new cases of tuberculosis were found (Gram (153)). On the other hand, Berghoff (154) reported 6 healed or quiescent cases activated out of 13 tuberculous soldiers in an army hospital.

Borst (155) reported 133 deaths following influenza, 33 of which were of soldiers. In all, 11 showed fresh tubercles traced to older foci recently inflamed. Altogether, 49 had old chalky deposits in lymph glands or cicatrices in the lungs.

Amelung (156) records the fact that in 36 cases influenza revealed tuberculosis for the first time, and in 21 patients there were no previous symptoms traced.

Kayser-Peterson (157) saw 7 cases of tuberculosis aggravated and believed that influenza caused new tuberculous processes to develop about the centre of the lung.

O'Reilly (158) considers that of his 416 cases of tuberculosis, 112 began with influenza.

Würtzen (159) treated 26 cases of tuberculosis developed by influenza, of which 20 were of an acute type.

Kieffer (160) cites 30 cases in which immediately or after some weeks following influenza a severe, acute, and in many cases fatal tuberculosis ensued. Many were previously strong healthy young people, and both sexes were represented. Others already known to have a history of tuberculosis, or suspected of it, when relapsing on account of influenza were markedly milder and more favorable in their course.

Mason (161) reports as a result of a survey of 7058 persons in Cincinnati on the after effects of influenza, that the 183 tuberculous cases discovered were nearly all new and hitherto not reported to the board of health. Only 61 were confirmed by sputum or X-ray findings, however,—less than 1 per cent of the total.

Douglass and Brown (162) give a report on the Ohio State Sanatorium experience. Of 615 patients admitted since 1919, 40 per cent attributed their active symptoms to influenza, and of these latter 67 per cent had no history of tuberculosis previous to the epidemic of 1918; the remainder, 33 per cent, were classified as reactivated. Of all the patients, 62 per cent had a positive sputum.

Sloan (163) collected statistics from twenty-nine sanatoria and tuberculosis hospitals in the United States, covering 7871 "bona fide" cases of tuberculosis admitted from October 1, 1918, to October 1, 1919, and 27 per cent of these had suffered from influenza. Of these, 54 per cent, or 15 per cent of the total, gave a previous history of clinical tuberculosis. Boisliniere (164) found the same percentage in 409 cases of proved active tuberculosis admitted to Mount St. Rose Sanatorium.

Heise (165), from the histories of 251 patients admitted to the Trudeau Sanatorium from October 1, 1918, to October 1, 1919, traced the onset of their disease to influenza in 52 cases. One-half of these were positively diagnosed who had no symptoms prior to the influenza. Nine cases were found to be nontuberculous, leaving nearly 10 per cent of all admissions chargeable to influenza.

Making due allowance for mistaken diagnoses in the clinical statistics, the combination of influenza and the strain of the war in 1918 furnished a large harvest of active tuberculosis which is still being reaped.

Nearly all sanatoria reported vastly fewer cases of influenza among their patients under treatment at the time of the epidemic. Some, indeed, ascribed this fact to a relative immunity possessed by the tuberculous. There was, however, little evidence of this among those who were under the normal conditions of life and its strain, and ignorant of their tuberculous infection. The time is still too short to estimate the number of active cases of tuberculosis fairly chargeable to the first epidemic of 1918. Sanatorium statistics alone will not suffice, because many of the tuberculous do not come under their care and often no diagnosis is made.

Moreover, there is a large number whose active symptoms are transitory and if known will be concealed or forgotten, possibly never to return. It is sufficient here to point out the coincidence, if nothing more, of influenza and tuberculosis.

It is unnecessary to dwell on the connection of measles and whooping cough with the activation of tuberculosis. They relate for the most part to children and youths who may be supposed to harbor recent tuberculous infection. Therefore, they may really be considered intercurrent diseases in the course of a developing tuberculosis, aggravating the inflammatory process in the lymph nodes and mechanically (by coughing) hastening the blood and lymph stream. Other explanations are also advanced to account for tuberculosis developing after diseases like the exanthemata, influenza, typhoid, etc. They are comprehended under the term anergy, in contrast with allergy, the term coined by von Pirquet to denote the changed reaction after infection.

ANERGY

Efforts have been made to explain activated latent tuberculosis on an immunological basis. Von Pirquet first called attention to the loss of tuberculin skin sensitiveness during the height of an attack of measles. The same phenomenon was noted during scarlatina by Rolly (166), and at the height of influenza in children by Shiff (167). This was observed by Berliner (168), Müller (169), and Bloomfield and Mateer (170) in adults. Nobecourt and Paraf (171) made Pirquet tests on 100 pregnant women at different periods, and after delivery made weekly tests. In 15 of 68 positive reactions, there was a disappearance or diminution of the reaction after labor, which returned in twenty-five to thirty-five days.

It cannot be denied on theoretical grounds .that when the specific resistance is depressed, as shown by the temporary loss of sensitiveness, it can be a factor in permitting living bacilli to spread. It seems to us, nevertheless, that it is too temporary to be important, or at least that it is of secondary importance to the mechanical dissemination of the bacilli. In fact Berliner (168) still obtained positive complement fixation reactions in the blood of patients who had lost the skin response.

When the new foci are formed their character may well be influenced for good or ill by the weakened reaction of the tissue cells.

A prolonged delay in the response to tuberculous reinfection can be understood and is probable in the presence of extreme debility such as occurs after exhausting illness, hemoptysis, etc. Holmes (172), however, showed that tuberculin sensitiveness was high at the clinical onset and became higher as the disease advanced. It is well known, of course, that sensitiveness diminishes in the terminal stages or in acute miliary tuberculosis. On the other hand, a diminution or loss of reaction after healing of tuberculosis is undoubtedly a favorable omen.

The matter is highly complicated and we are prone to speak of "reduced resistance" without a clear conception of its mechanism in accounting for an activated tuberculosis. We recognize this state in diabetic and malnourished persons; likewise in those who undergo nervous, emotional or mental stresses. The alarming increase of clinical tuberculosis in the warring countries brought into play nearly every factor in the accepted etiology of tuberculosis.

Anergy in this sense must be accepted without further definition. Antityphoid immunization was definitely associated with tuberculin anergy by Mayer (173) and with outbreaks of clinical tuberculosis in soldiers by Schröder (174) in 46 out of 62 cases, but Mayer saw no such effect in incipient cases.

Jacob (175) observed 106 cases of tuberculosis in soldiers, but none developed after the antityphoid inoculations; and in spite of the exaggerated press accounts in the United States no definite connection has been established. Coincidences must be taken into account in all observations of this kind.

The awakening of old foci in organs other than the lungs also deserves mention. It is in these cases of dormant disease in the joints, bones, genitourinary tract and meninges that the question of exogenous reinfection need not be raised. They are frankly metastatic except in a few cases of wounds of the skin directly inoculated from outside (Orth (119)).

In metastases the frequent rôle of trauma and excessive strain is plain. According to Orth bacilli may be brought to the site of the injury by the blood after as well as before injury, thus setting up new foci. Bacillemia nevertheless is not understood to be a recent exogenous infection, since it implies a focus elsewhere in the body in an active stage but of more or less remote origin as to time.

INFLUENCE OF AGE

The age when reinfection takes place from endogenous sources is one of the difficult questions. The sudden change in the incidence of tuberculosis at puberty offers a mystery because, as already mentioned, apical tuberculosis appears with a human type of bacilli whether the primary infection was the same or of bovine origin.

The main argument for successive endogenous implantations must rest on the gradual or intermittent development of pulmonary tuberculosis as seen in its clinical aspects and by X-ray examinations. Where the new lesion adjoins old foci or is on the same side, as in chains of old tuberculous lymph nodes, for example, in the neck, the opinion is strongly in favor of an endogenous extension of the disease. These are the most evident cases and they are often favorable for arrestment, or drift into middle life as chronic types of the disease. The question whether exogenous reinfection adds new and more virulent bacilli to such lesions cannot be seriously raised when the progress of the disease is traced step by step. The acute type of pulmonary disease in youths is less easily associated with endogenous sources of long standing. Ascher (176) holds that school age may represent the highest point in natural resistance as well as that acquired from infection. The pulmonary disease from this age upward increases in frequency. Some will explain this by endocrine gland activity or subtle changes in the nervous system at puberty. Susceptibility dependent upon overstrain and exposure is certainly associated in the causation of the active disease in youth, but the special causes of susceptibility, if any, are undefined.

Tuberculosis in old age is readily ascribed to metastases of past infection for the most part and is rarely acute. Offenbacher (177) studied 102 cases over forty years of age: 27 per cent gave a perfectly healthy history; the others could be traced to previous periods; in 23 hemoptysis was recorded, ranging from the tenth to the seventieth years.

The complex influences brought to bear on the vitality of individuals and their family, community and racial life as causes of the activation of the latent bacillus, need not be entered into here. It is well to refer to them, as they are of tremendous moment not only in the incidence of infection but in its further progress. The curve of tuberculosis morbidity rises with the increase of want and hardships, and falls with economic, physical and moral betterment.

Were it not for the persistence of the tubercle bacillus in the body and its ability to reproduce, the universal infection would not be unwelcome. The history of variolation, or preventive inoculation of variola, in the eighteenth century, so well described by Klebs (178), is a lesson not to be lost in its application to tuberculosis.

The deaths caused by the variola inoculations were but 1 in 200—vastly less than from the disease spontaneously acquired. Bushnell (179), in his recent work on the epidemiology of tuberculosis, boldly advocates universal tuberculization by a weak inoculation, repeated sufficiently often to maintain the relative immunity. Such an idea has long been held, but it disregards the other factors in the causes of tuberculosis as a disease which might awaken virulent qualities in the vaccine.

SUMMARY ON ENDOGENOUS REINFECTION

The first object of assembling the preceding references to clinical and pathologic examinations is to make known the great number of unsuspected tuberculous infections of the lung apices, especially in young adults. The proportion of cases involving the other lobes is indoubtedly considerable, but it is the apical involvement that represents the typical adult type of the disease, and which is most easily distinguished from primary childhood infection. We are therefore justified in regarding them as secondary or reinfections of exogenous source, unless we can connect them in some way with early primary infections which have never healed beyond the chance of reactivation.

We have little proof that the calcified obsolete tubercle is capable of much mischief and we know that the bovine bacillus is found in about 10 per cent of the first infections but almost never in the sputum from adult human disease. Then there is often so great an interval between the first infection and the ultimate pulmonary disease that we cannot bridge the gap with any history of symptoms. In deaths from other diseases pathologists do not often find tubercles in an "active" stage; yet small deposits are frequently found in the apices, although not of the caseous type as a rule. They are more frequent as age increases, so that the suggestion is strong of an exogenous source. If, however, the first infection was sufficient to set up secondary foci slowly spreading by way of the lymphatics or by the blood stream to the periphery of the lung, we are then faced with the probability that endogenous metastases account for later disease.

We have presented some statistics from sanatorium records and other investigations which suggest that from 20 to 80 per cent of clinical tuberculosis from the fifteenth year upward is derived directly from childhood infection. These estimates are so divergent that one must conclude that the methods of inquiry vary too greatly, or that the results are influenced by personal bias; a safer estimate would be based only on those who have definite family exposure before the age of fifteen years.

From the recent military experiences it is deduced that some acute cases were freshly infected, but that the great majority of them were endogenous, reactivated from previously acquired infections. It may also be assumed that the dosage and virulence of autogenous bacilli will be greater than any others.

The results of the United States army and draft board examinations, the community surveys, and the clinical and pathologic experiences, all tend to establish the presence of a vast number of inactive pulmonary cases in our city populations. When did they begin and whence were they derived?

Before discussing the problem further let us consider exogeneous infection, its sources, amount, and the conditions under which it may be expected to occur.

REINFECTION FROM EXTERNAL SOURCES (EXOGENOUS REINFECTION)

The students of tuberculosis have represented all shades of opinion on this problem, the majority having given little attention to it until Römer's views were advanced.

Theobald Smith (180) has viewed the subject from the angle of changes in the parasitic power of bacteria; that the bacilli having acquired this power in the tissues of one host are able to infect others at any age. The statistician, Karl Pearson (181), considers that heredity plays a large part in transforming infection into disease. Neufeld (182) inclines to the belief in a high immunity for adults against small amounts of inhaled bacilli, but considers Römer's position not completely established for human subjects. He thinks it easier to protect animals against a single large infection than a number of small ones such as presumably occur in man. The British epidemiologist and statistician, Brownlee (183), mentions his acceptance of the theory of immunity conferred by childhood infection which, however, breaks down and causes two-fifths of adult phthisis from endogenous spreading. The inference is that three-fifths must be from exogenous sources. Fishberg (184), in a study of marital infection, positively disbelieves in adult reinfection.

Bushnell (179), who quite recently in his book on epidemiology has traversed in a very complete way the literature of racial differences in incidence and types of tuberculosis, strongly favors the theory of adult immunity in consequence of early infection.

Calmette, in his comprehensive new work (36), accepts exogenous reinfection as superimposed on the old infection, and holds that, commensurate with its amount, virulence and close sequence, it gives rise to the Koch phenomenon of ulceration leading to open tuberculosis. The chief danger, in his opinion, lies in repeated infections which finally produce a chronic disease. Acute forms of tuberculosis, not traceable to old foci, are generally regarded at present as primary infections, and these are seen especially in persons from isolated, sparsely populated places or in primitive peoples.

The pathologists have demonstrated an increasing percentage of tuberculous foci in the lymph nodes and lungs from childhood to the age of universal infection in civilized peoples, which is between the fifteenth and twentieth years.

From this it is evident that the first infections are not all in childhood or in immature youth. The later ones are possibly more liable to be held in the lungs, and do not affect the lymph nodes of the hilum. Our experiments lend support to this view. From year to year, successive inhalations of bacilli, if they succeed in entering the tissues, would be expected to arouse a different reaction in the tissues and one that is prone to healing or to progress in a chronic form. In other cases the subjects of the invasion fall victim to an acute tuberculosis, but in decreasing numbers as age advances.

Astonishingly few cases outside of tuberculous families can be traced to definite sources of infection, and relatively few of these pursue the acute course of a primary infection as seen in the primitive peoples. In the first place we may point to the difficulty of finding large numbers of bacilli in the air of infected rooms. Collections of dust and droplets sprayed by talking, coughing, etc., are indeed found to contain bacilli but in small numbers and (at least in the dust) with reduced virulence.

The examination by Straus (185), Möller (186), and others of nasal secretions from nurses in tuberculosis hospitals was definite proof that living bacilli were being inhaled, but the proportion of bacilli received at any single exposure must be regarded as small. The sputum of nontuberculous persons under exposure to hospital or sanatorium patients has often been examined because of a suspicious cough or catarrh, with negative results. If bacilli were very numerous in the vicinity of such patients they should be found in the tracheal secretions, like the smoke particles so familiar after a railway journey. We think this consideration is lost sight of in most essays on infection.

In the instances of close and prolonged contact of near relatives, where the droplet infection opportunities are inevitable, it cannot be maintained that at any given day or week a large dose of bacilli must necessarily be inhaled or swallowed. The amount in the course of time may theoretically be considerable under extreme exposure, but the demonstration is wanting. The majority of the particles of sputum rich in bacilli are too heavy to be inhaled at all; they fall to the floor or bed and become dried before it is conceivable that they can be again air borne.

The experimental work of Flügge and his associates (187), in our opinion, cannot be adduced to prove what is imagined to be "massive" infection by moist droplets.

It was well demonstrated by Nenninger (79) and Paul (188) that the finest vapor could carry bacteria to the deeper parts of the lungs through the smallest divisions of the bronchi; but, as Paul states, the number of bacteria reaching the alveoli will depend upon the proportion contained in the vapor. If the danger from inhaled dust containing large numbers of tubercle bacilli be considered greater, which we cannot admit, the theoretical number will be larger than in droplets. Together with droplets, dust particles could make the total dose large, but the reduction in virulence by drying must be considered.

In the second place, inhalation infection must overcome powerful natural defenses. There are the ramified nasal passages with their cilia and the strong outward movement of particles inhaled directly into the deeper bronchi. According to Thompson and Hewlett (189) the cilia of the human nose expel bacteria in two hours. Paul (188) found a rapid decrease in the numbers present in the lungs of rabbits by testing one and one-quarter, two, six, and seventeen and one-half hours after experimental inhalation. In brief, a healthy condition of the air passages presupposes a fairly constant clearing out of foreign particles. In the examination of large animals immediately after slaughter Quensel (190) found few bacteria, and in 4 sheep out of 15 the lungs were sterile. More than half the cultures from tracheobronchial lymph nodes of calves, sheep, horses and cattle were sterile. The nasal and bronchial mucus has also a protective function, in the opinion of some investigators, by reason of its unfavorable qualities as a bacterial culture medium. If any influence is exerted by the mucus on tubercle bacilli it is probably mechanical rather than inhibitory.

The conclusion about direct droplet and dust infection is, therefore, that it deals with small numbers of bacilli, and in ordinary health the massive doses are for the most part carried outward by the normal defenses without entrance to the tissues.

It remains to consider what factors may aid inhaled infection. From the mechanical standpoint there is much to invite thoughtful attention. From the time of infancy, when the prolonged cries are followed by deep inspirations with the wide open mouth, to the romping school child and youth rushing into the house breathless from running, there are always chances that bacilli may penetrate far deeper than usual. Then follows the age of competitive athletics, indoors as well as out; the social games and dancing, often accompanied or followed at all ages by catarrhal colds, nasal obstructions and fatigue—in short, the deep breathing in an infected atmosphere which courts danger of further infection while tending to mobilize previous infections.

Calmette and Grysez (191) showed that inhaled bacilli may be taken into the alveolar spaces by leucocytes migrating, thence to find their way to the lymph spaces. When bacteria are inhaled beyond the reach of cilia, their removal becomes a much slower process through absorption as foreign particles, and cumulative infection can be understood from the increment of virulent bacilli added in small numbers from day to day.

Here we can understand the hereditary influences playing a part in the process above described. The *habitus phthisicus*, in so far as it is not brought about by early infection or malnutrition from the same cause, furnishes conditions tending to hold the bacilli in the lungs; that is, the pulmonary ventilation is poor and the blood-lymph circulation slower in the malformed chest.

If all of these considerations are valid so far as they apply to inhalation infection, there is reason to think that exogenous reinfection may be fairly frequent in the young, but in relatively small amounts,—conceivably much less than ingested infection from soiled hands and food. When full growth is established we have the added problem of the influences of occupational strain, pregnancy, and the previous infections. Pulmonary apical tuberculosis then becomes the predominant form of disease and no evidence of bovine reinfection complicates the picture at this age.

A large percentage of the clinically active cases cannot be traced to to recent close contact with or prolonged exposure to an environment of tuberculous infection; neither are they all people of uncleanly habits. In the latter respect swallowed infection is not seriously considered in civilized adults.

The sudden drop in the incidence of bovine infection at puberty points to a similar conclusion. The rarity of intestinal tuberculosis except from autogenous sources leads us to focus attention on inhalation, and forces us to look for some special vulnerability of the lungs. As to this speculation has much, but demonstration little, to give us.

On the other hand, the mass of the adult population, many being in frequent contact with coughing consumptives, fail to develop clinical pulmonary tuberculosis, if indeed they become reinfected at all. There is also no experimental evidence that reinfection by inhalation directly selects the cranial lobes of the lung. It is quite well accepted that by way of the blood and lymph stream this does happen, but whether from recent or previously acquired infection cannot be answered in each case. Since the upper air passages must also be regarded as avenues of reinfection, the matter is further involved.

SUMMARY

In the face of such complexities it is presumption to marshal the known facts into a law applicable to all cases of a disease exhibiting such great contrasts.

The medical world seeks for a formula, or creates one according to the degree of dogmatism of its author. Then comes a world war and its aftermath of disease and privation; the formula does not apply, and confusion reigns again. It is indeed a disquieting thing to contemplate the reported large increase of tuberculosis in Europe and then point to the steady fall in mortality from this disease up to the war years as due to the suppression of the tubercle bacillus. Moreover, the abrupt fall of the tuberculosis death rate in this country since the influenza pandemic has puzzled those who predicted a large increase of tuberculosis following the war and the pandemic. Harmonizing these experiences presupposes more knowledge than we possess, yet not all is mystery.

There is a period between the date of infection and the recognition of tuberculosis as a disease that is lost to us in too many cases. The symptoms are absent or too vague and fleeting for our present methods of detection. There are, it is true, the earliest hemoptyses without other symptoms, the definite pleurisies,[8] not to mention the external forms of tuberculosis possible of early discovery.

The *postmortem* not infrequently reveals a group of fairly early tubercles in the lung parenchyma, and oftener well marked tracheobronchial involvement of uncertain age, in individuals dying from other causes. These are not, by any means now at our command, connected with a definite period of time of infection, unless we are to except children.

There are primary infections, progressive and fatal at all ages. In the races recently brought into contact with tubercle bacilli, the matter offers the simple explanation that there is no resting period once the infection has begun to spread. The elements of dosage and frequent cumulative infection must be considered in these cases, because of the manner of life of the people.

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[8] Neumann (192) describes a group of vague signs and symptoms that he considers diagnostic of primary lung infection.

Where acute primary tuberculosis is suspected in an adult of the white race and of cleanly habits, there has been a tendency to assume an an unusual virulence of the bacillus, ignoring the possible absence of resistance from lack of previous infection. Certain families have been devastated by acute tuberculosis where we should expect early infection and, from the relative immunity thus acquired, a slower course of the disease. It must be remembered that not all the individuals in such families do in fact exhibit such acute forms of the disease and some, perchance, escape altogether. These again are the puzzling contradictions.

We return, therefore, to the main fact of universal infection, single or repeated, for an interpretation of all these variations.

It is evident from what has been presented in the experimental and pathologic study on man and animals that successive infections do occur, and that the first often modifies the course of the later ones.

In comparison with the ease with which a primary infection is acquired, the later inhaled and ingested bacilli are resisted more or less strongly by the relative "immunity from infection."

In applying these principles to human tuberculosis we note many evidences of confirmation which in the main are satisfactory. There are reasons to suspect mild infections, both as to quantity and virulence, occurring infrequently but by a cumulative effect ultimately arousing the disease process.

The earliest exogenous reinfections are probably often well resisted and may produce no noticeable symptoms.

Good physiological functions combined with the immunity from infection tend to ward off further infection after adult age is reached. Should the conditions be otherwise than favorable, or the infection frequent or potent, disease results.

We have discussed the unlikelihood of massive infections by inhalation, and the doubt about other ways of reinfection. From the very small quantities taken in at one time and the slow development of the disease we are inclined to the theory of cumulative infection during childhood and youth.

The majority of individuals who are to develop pulmonary tuberculosis for the first time after the age of twenty have already acquired it to a degree. Were it possible to discover these potentially diseased cases, who may or may not break down, we believe there would be but a small percentage not accounted for among the victims of tuberculosis in civilized countries.

It is virtually impossible to associate many cases of clinical tuberculosis in adults with a recent exogenous source of infection, except under family exposure. Even in family disease, as is well known, the patient often develops the first recognized symptoms years after the death of the relative.

Many similar observations might be brought forward to show the futility of trying to place the date of infection, except in those adults (either of primitive races or others) hitherto unexposed because of complete isolation. The town or city dweller is a survivor in the sense that he has reached maturity in the face of more or less inevitable exposure to human and bovine infection.

The results of wholesale physical examinations are impressive in the number of unsuspected pulmonary cases in fair health. What happens to many of these may be surmised from the increased mortality during the war, and from the sanatorium records of relapse. Under strain and with an acute influenza, others have come to knowledge but are not yet recorded in the mortality tables.

The steady decrease of tuberculosis for years antedating the great war has been variously interpreted, but from the revelations above mentioned concerning the large number of undiscovered cases we are obliged to confess that the lessening of opportunities for infection has not been accomplished to the extent desired. Yet we are persuaded that the frequency and quantity are lessened.

Meanwhile the standards of life had improved, tending to prevent both exogenous and endogenous additions to the already acquired infection, thus increasing the number of healed cases. Then came the war and its hardships, exposure and starvation. Thousands of arrested or partially arrested tuberculous persons have relapsed and their disease become progressive. Deaths were hastened, and together with influenza the work of years seemed wasted by the war.

The amount of disease during the war attributable to reinfection cannot be estimated, but it is safe to say it was but little in the armies. With the crowding of the cities by workers and the combined strain we should frankly expect many new infections.

To sum up our study of this problem, we believe that the lesson to be learned and applied is that, hand in hand with efforts to safeguard the young from infection, more attention should be paid to safeguarding both young and old from disease.

Without sputum and dairy hygiene the supply of dangerously infected young people will be kept up; without earlier diagnosis, education, and favorable conditions of life for the prospective victims, clinical tuberculosis will continue at an irreducible minimum.

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SOME CAUSATIVE FACTORS OF PULMONARY TUBERCULOSIS[1]

LAWRASON BROWN

In discussing before you the etiology—the cause— of pulmonary tuberculosis, which accounts for 87 per cent of all the deaths from tuberculosis in the United States, I am more at my ease than I could be with any other topic connected with pulmonary tuberculosis, for no matter how bizarre my statements may be, I might quote opinions and even experiments to prove that they are right.

As time flies on, we are all impressed by the fact that many utterances relating to this subject, often *ipse dixit* in character, are sustained not by proof but by weight of authority. In fact, we have had thrust upon us so many half truths, that if we seriously consider the whole problem to-day we find that students of pulmonary tuberculosis are in complete accord upon only one fact, established thirty-nine years ago, namely, that pulmonary tuberculosis is due always to the presence of tubercle bacilli in the lungs. At first thought, the etiologic chain seemed complete. The tubercle bacilli grew and multiplied in the lung, producing, as the disease progressed, ulceration into the bronchi, through which bacilli escaped into the open by means of the sputum, which was formerly deposited much more freely and carelessly upon floor, platform, or sidewalk than it is to-day. From these places the bacilli somehow gained entrance into the body of a new host. So, to prevent the spread of the disease this cycle must be broken at some point, which in the earlier days seemed simple enough to do.

It was but natural for Cornet to attempt to prove that the usual method of transference from man to man is through the inhalation of the fine particles of dried tuberculous sputum waited about as dust.

For years this was accepted as the usual means of inanimate transmission. But patients, Flügge said, when they cough emit a spray of coarser and finer and almost impalpable particles of sputum that fly to a distance of three to four feet from the mouth and may remain suspended in the air for about a half-hour. This, as the usual method of transference, was for him far more important than dust. More recently these so called inhalation methods of infection have been questioned as far as they can be considered the usual method of infection. Krause would emphasize the importance of raw sputum, contaminating the hands of young children through balls, hoops, tops, etc., used in play upon our streets, while Cumming would emphasize that eating utensils, particularly spoons, which our younger children use almost exclusively, are in his opinion the chief conveyers of infection, for ordinary washing by no means sterilizes them.

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[1] An address delivered before the school of Hygiene, Johns Hopkins University, March 14, 1921

However it occurs, we know that a large proportion of the urban population, at least, harbor the tubercle bacillus by the time they reach puberty. This might be stated as a second uncontrovertible fact.

But from this time on we again encounter divergent views. Some would have us believe that all pulmonary tuberculosis is due to the further progression of a childhood infection and that adults are practically never reinfected. On the other hand there are those who maintain that while this does hold true in a certain proportion, say in 50 per cent of the cases of adult pulmonary tuberculosis, in the other 50 per cent pulmonary tuberculosis is due to adult infection. In either case infection is not synonymous with disease, and it must be explained how so large a proportion of infected individuals never develop frank disease. Here it seems to me that we must separate, as clearly as possible (which is not often done), those causative factors which bring about infection from those which bring about the development of infection into clinical disease. It may be stated briefly at this point that any circumstance that upsets a bodily balance which has prevented tuberculous infection from advancing into tuberculous disease is, of course, a causative factor. I refer among others, to overwork, poor hygienic surroundings, poor food and certain diseases.

I have mentioned two basic facts that we can all agree upon: first, without the presence of the tubercle bacilli in the lungs there can be no pulmonary tuberculosis; and, second, by the age of puberty a large majority of children (70 per cent) harbor or have harbored the tubercle bacilli in their bodies, more particularly if they dwell in cities. By the age of twenty-five somehow all have been infected with tubercle bacilli.

I should like to divide my further remark into a discussion (1), of the tubercle bacillus, the parasite that causes the disease and (2), of the host, the human being, that is diseased.

THE PARASITE: THE TUBERCLE BACILLUS

This suggests a brief consideration of the tubercle bacillus, the parasite, which brings about infection and later, under certain conditions, disease. This germ has been held to have feeble powers of attack, if I may so term it, but great powers of resistance, thanks to its waxy framework. It is nonmotile, and depends upon the bodily functions to transport it within the body and upon air currents and inanimate objects for movement without the body. It was formerly thought to be ubiquitous but recently studies have not upheld this view. However this may be, all of us sooner or later come in contact with the tubercle bacillus and many of us meet it frequently. It is of interest to see where it lurks outside the body and to trace if possible its path from cow or man to the ill fated individual who develops pulmonary tuberculosis.

The bovine tubercle bacillus. The danger of tuberculous meat is practically nil; but the danger of milk containing bovine tubercle bacilli is more real, and can be roughly estimated in two ways: first, by noting what percentage of human beings suffer from bovine tuberculosis, and, second, by observing the effect of contaminated milk upon individuals who have imbibed it.

Figures collected in 1911 by Park and Krumwiede show that in 1224 cases in which the type of tubercle bacillus was determined, the bovine tubercle bacillus caused 4.3 per cent (that is, one case in 24 examined) of pulmonary tuberculosis occurring in children and infants under five years of age, none in patients from five to sixteen years (11 cases), and one in 645 cases of adult pulmonary tuberculosis. In other words, bovine tubercle bacilli caused pulmonary tuberculosis in only 2 of 680 cases, less than one-third of one per cent, a figure that appears almost negligible. In a collected study of the type of the bacilli in the sputa in 938 patients with pulmonary tuberculosis, at least three were found to be of bovine origin (Griffith), one was doubtful and two were mixed. In any case, far less than 1 per cent and in all probability less than one-half of 1 per cent were thus due to the bovine tubercle bacillus. Do not misunderstand me: bovine tubercle bacilli produced the disease that killed nearly one-fourth (23 per cent) of the 280 cases of all forms of tuberculosis occurring under five years of age, slightly more (24 per cent) in the 153 cases between the fifth and sixteenth year of life, but only 1.3 per cent in adults. In this group of figures pulmonary disease occurred in 82 per cent of the cases in adults, in 7 per cent between five and sixteen years, and about in 9 per cent of children under five years.

Two years later (1913) Kossel collected the figures of various observers in all countries and found that in 832 cases of pulmonary tuberculosis, three were due to bovine, two to bovine and human, and one was badly defined, or in other words, in over 99 per cent (99.3 per cent) of all cases of chronic pulmonary tuberculosis, the disease was caused by human tubercle bacilli. From these figures, then, the importance of bovine tubercle bacilli in pulmonary tuberculosis in man is at the most but slight.

The mutation of bovine tubercle bacilli. The mutation or transformation of the bovine into the human type of tubercle bacillus has been frequently suggested. From the figures I have mentioned it can be seen that up to puberty bovine tubercle bacilli are frequently found, but after this age they occur so rarely that some have suggested that they are transformed into the human type. This change of mutation has never been proved. I have never been able to find any study which determined whether or not a bovine infection persisted before, through and after puberty. The infinitesimal additions of certain substances, that bring about marked changes in colloidal states, suggest that at puberty certain changes might occur in the bodily tissues that render them no longer suitable for growth of bovine and possibly more suitable for the growth of human tubercle bacilli. This is in part borne out by the fact that bovine bacilli grow less readily than human bacilli upon artificial media and require slightly less acidity, or lower hydrogen ion concentration, as it is termed to-day. Thousands of adults must drink tuberculous milk daily and while thus exposed they apparently almost never develop bovine disease.

It is common knowledge that bovine tubercle bacilli do occur in cow's milk and in some specimens it has been estimated that one-half million tubercle bacilli are contained in one teaspoonful of milk. It has been found that 16 per cent of the specimens of milk examined in New York (in 1910) contained tubercle bacilli; 10.5 per cent in Chicago (in 1910); 7 per cent in Washington; 22 per cent in London; and 20 per cent in Edinburgh. In Berlin 619 persons (284 children, 335 adults) who had drunk raw milk from cows with tuberculosis of the udders were studied (A. Weber). Only 2 children were clinically tuberculous (both had cervical adenitis). Of 18 children (9 under two years, 8 from two to five years and one more than five) exposed in a similar way, only one became clinically tuberculous (it also had cervical adenitis); and but 4 reacted to the ophthalmic tuberculin test. In fact, in regard to the danger of tuberculous milk we are led to conclude that only when children are fed constantly with milk containing large quantities of tubercle bacilli is the danger great, and as milk bought in large cities comes usually from many herds, the quantities of tubercle bacilli are usually not large. These facts, however, do not relieve us of the necessity of obtaining milk for our children from tuberculin tested herds or of pasteurizing it before use, for from 8 to 10 per cent of all tuberculosis deaths in children are due to the bovine tubercle bacillus.

The human tubercle bacillus. Now if we can exclude the bovine tubercle bacillus as the cause of chronic pulmonary tuberculosis in adults, and I think the figures I have presented to you enable us to do so, we can concern ourselves entirely with the human type. In other words, practically every patient with pulmonary tuberculosis has been infected either directly or indirectly by another patient. How do these bacilli pass from person to person?

We know that the sputum of patients with advanced disease may contain enormous numbers of bacilli. Professor Nuttall of Cambridge, formerly connected with this University, estimated that the sputum could contain as many as one to four billions of tubercle bacilli in twenty-four hours, and Heller estimated that a patient could expectorate over seven billions of tubercle bacilli in the same time, though all of these are probably not alive. With the prevalence of tuberculosis which has existed for years, along with the former belief that tuberculosis was hereditary and not contagious, and with the careless disposal of the sputum in use for years, it seems almost incredible that many more did not succumb to pulmonary tuberculosis, if the tubercle bacilli in the sputum could be distributed as some would have us believe.

The danger of dust. I have referred to Cornet's work which he believed went to show that tubercle bacilli were carried from man to man by means of particles of dust. The patient spits upon the sidewalk, upon the floor perchance, and the unwitting carrier bears the bacilli on shoes or skirts into the house, there to deposit them upon the rugs or carpets. The sputum dries and, according to this theory, is ground into dust which the careful housewife cannot bear to see at rest. So literally she dusts not only the floors, the furniture, but also the lungs of those who dwell therein.[2] On a tiny particle of dust, visible only when it dances in the sunbeam, ride perchance twenty or more tubercle bacilli along the various air currents, to find finally a resting place in a tiny ramification of a bronchial tube, deep in the interior of the lung. Here, in some instances, the bacilli proliferate; some would have us believe in the air passage itself; others (and this is more probable) only after they have penetrated the mucous membrane and gained access to the intrapulmonary masses of lymph tissue. Their growth and the resultant destruction and compression of pulmonary tissue ultimately bring about clinical pulmonary tuberculosis.

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[2] It is of interest to note in passfng that many housewives contract tuberculosis but the percentage of housewives form a large part of the female population.

That bacilliferous sputum has been in the past and still is widely distributed on our sidewalks, on platforms, on the floors of public buildings and elsewhere, cannot be denied. Such sputum can be used to infect guinea pigs. But aside from this what do we know of the existence of human tubercle bacilli outside the body? Innumerable experiments have been performed to show how long the tubercle bacillus can resist light, air and drying. Direct sunlight or sunshine is supposed to kill tubercle bacilli in thin layers of sputum in a few hours (four to six), while indirect sunlight may require several days to do so. Fresh air, even in the absence of sunlight, has caused their death in a few days: combined with sunlight it would work more quickly. Dessication is also injurious. When in masses of mucus, however, tubercle bacilli may be protected from the effects of light and of drying which render the mucus a tough or hard mass. So tubercle bacilli deposited upon our streets in large masses of sputum, especially in coarse dust and sand, may resist for days these destroying forces. It is interesting to consider then what happens to a mass of sputum which is trodden under foot on a sidewalk. While contaminated shoes may track it into the house, the mere fact that it has been spread out over a fairly wide area renders the tubercle bacilli that remain upon the street far less resistant, and in my opinion greatly hastens their death. I can conceive how a shoe contaminated by such sputum several blocks from home can be of danger or a source of infection, particularly for young children who play about their elders.

Mr. Petroff, Dr. Pesquera and I poured some sputum containing innumerable tubercle bacilli on a board, trod upon it and then trod on and wiped, so to speak, our shoes on a piece of carpet. After some hours the carpet was placed in a small box containing several guinea pigs, and a stiff, rotary brush attached to a motor was set in motion and kept running for some hours on several different days. None of the guinea pigs became infected.

Samples of dust from many locations, both indoors and out, have been searched for human tubercle bacilli and injected at times into guinea pigs, all with varying results (18 per cent to 48 per cent were positive (Cornet)), but experiments made with the dust that leaves the floor after ordinary dry sweeping, that is, with the dust we ordinarily inhale, have proved it infectious far less often (8 per cent). It may be stated that, when tuberculous sputum becomes dried and ground into dust out-of-doors, the tubercle bacilli are so weakened that they are of little danger or else are killed. House dust may be much more dangerous and to-day many hold that tuberculosis is practically always contracted indoors. The statement that pulmonary tuberculosis is a house disease must embrace this fact; but it must also be remembered that families that hover about the poverty line often sink into the same wretched living quarters. Under these circumstances lack of food may be as important as exposure to the infectious dust left by a previous occupant. Such conditions, it appears to me, have often less to do with infection than with the development of disease from previous infection.

Mr. Petroff, Dr. Pesquera and I also tried to find tubercle bacilli outside the body in Saranac Lake and at the Trudeau Sanatorium. Two rooms occupied by patients with violent coughs, both of whom have since died, were carefully examined in regard to the dust upon the floor, the walls, the bed table and the chair, but no tubercle bacilli were found either by staining or by inoculation of guinea pigs. This confirmed the finding of a former assistant, who, hoping to show that tubercle bacilli were present in the dust of a room in the infirmary at Trudeau, occupied by a patient with numerous tubercle bacilli in his sputum and an explosive violent cough, inoculated the dust into a guinea pig with negative results. Having found no tubercle bacilli in the dust of rooms by the use of swabs, we constructed a glass chamber, just large enough to hold a guinea pig and attached it to a vacuum cleaning apparatus which drew the dust of the room past the guinea pig for one-half hour. Guinea pigs we thought, might contract tuberculosis through inhalation when inoculation failed, but the three guinea pigs used remained free from tuberculosis. Much emphasis has been laid upon the danger from the mouth pieces of telephones, but dust collected from the public telephone at Trudeau failed to infect guinea pigs. The dust collected from a large rug in the general assembly room at Trudeau also produced no tuberculosis on inoculation.

These experiments led us to conclude that, with the prophylactic technique in use at Trudeau and Saranac Lake, the dust of rooms was no source of danger. It must be remembered, however, that if the consumptive spits upon the floor, it is very likely that the dust from the room will infect a guinea pig, which Hance proved many years ago at Trudeau. Virulent tubercle bacilli have been found in the dust of a room six weeks after the death of a consumptive, but usually at the end of six months all infectivity has gone.

The climate which stimulates us, which gives us our energy, which in short makes Americans of us, has an untoward effect upon our mucous membranes, and whether we dwell at the sea coast or on the high, dry western plateaus, we suffer more or less from catarrh and so are led to spit. The antispitting crusade has done yeoman service and as soon as the general public realizes that their health demands that sidewalks, street crossings and floors be kept free of all sputum, we shall see reductions in mortality from all respiratory diseases.

The danger of droplets of sputum. Some years ago Dr. Baldwin and I built a glass box, into which we had patients cough, and found an occasional droplet of sputum containing tubercle bacilli deposited up to a distance of about three feet. Dr. Trudeau had found tubercle bacilli in the droplets of sputum on his eye glasses after a patient had coughed in his face. These droplets of sputum may therefore contain tubercle bacilli. It had been shown by Flügge and others that they may be sprayed to a distance of three feet or one metre from the lips of the cougher and remain suspended in the air for thirty minutes or more. These seem to me to be uncontrovertible facts. But our problem is how much danger lurks in these minute droplets.

From what has been said of the viability of tubercle bacilli, it can be seen that in such droplets they are readily exposed to the destroying influences of light, air and drying. That they can persist alive, or at least remain infectious, even in the house for more than a few hours, seems to me most unlikely, though this has been questioned.

On the other hand, however, we know that fewer tubercle bacilli in the form of a moist spray are needed to infect guinea pigs; and possibly weakened germs, thus gaining entrance into the body, may produce more or less benign pulmonary tuberculosis. It would seem to be an easy thing to cough into the face of a guinea pig and so infect it. Hoping to reproduce as much as possible the conditions under which an infant lives with a tuberculous mother, we got two of our patients at Trudeau to fondle guinea pigs and to cough all over them during their morning pulmonary toilet. Both patients had numerous tubercle bacilli in the sputum but the guinea pigs remained free from disease. This is not an isolated experiment for others have had the same experience. Heymans, a co-worker of Flügge, had great difficulty in producing infection in guinea pigs and dogs by this method, even after hours of exposure to coughing consumptives. It should further be noted that less than 50 per cent of patients with pulmonary tuberculosis, even with tubercle bacilli in their sputum, cough out droplets containing them, and the number of tubercle bacilli contained in the droplets is only a very minute fraction of those in the sputum.

On the other hand, Hess of New York and Hamburger of Vienna would have us believe that an extraordinarily short period of contact is required to infect an infant, but fomites and infected objects may have played a greater part than was thought or known.

The danger then of droplet infection may be said to be limited to those droplets inhaled before settling upon any object and probably is much greater for infants than for older children or adults.

Common colds leading to acute bronchitis aid greatly in disseminating germs that occur anywhere in the respiratory tract. Tubercle bacilli may recur in sputum only during a cold.

The danger of contact. The spread of tubercle bacilli from man to man by direct or indirect contact has recently been emphasized. It has long been considered dangerous to shake hands with a consumptive. We selected two patients, with abundant sputum loaded with tubercle bacilli, and had them cough violently into their hands. The wash water from the hands infected guinea pigs, a point Baldwin had shown many years before. We then endeavored to see if tubercle bacilli could be transferred from hand to hand by shaking hands but were unable to do so. We repeated the experiment with large quantities of another germ (B. prodigiosus), and found that they could be passed along a chain of three or four persons by this means. It seemed to us fair to conclude that mere coughing into the hands was not enough for transmission by this method, but gross contamination of the hands by sputum, such as wiping heavily infected lips with the hands, might be. We could not spread contamination produced by coughing into the hands to another's hands by means of the door knob.

Objects that come in contact with the lips may be contaminated, for in some instances the saliva contains tubercle bacilli in considerable numbers. To study the danger that lurks in the kiss we had patients kiss a sterile glass dish (Petrie dish), and found the danger was greater in the early morning hours. We should have liked to have had the patients kiss a guinea pig, but we felt that even the amount of fervor that enters into kissing a glass plate might have been lacking with the guinea pig.

It has long been taken for granted that eating utensils that come in contact with the lips—glasses, cup, forks and spoons—are contaminated. This had been shown by Price and we confirmed his work. The recent epidemics of certain respiratory diseases at the training camps in various parts of the country have shown the great danger of insufficient washing of eating utensils, and particularly when insufficient and contaminated water was used.

Cumming, who has studied hand-to-mouth and utensil-to-mouth infection, has concluded that many respiratory diseases, including tuberculosis, are transmitted in this way. In fact, this he holds is the usual method of infection and he incriminates particularly the spoon. Ordinary methods of washing, he states, are insufficient to rid the spoon of tubercle bacilli, as he proves by guinea pig inoculation. Price, however, found that hand washings of utensils, followed by scalding, was enough to sterilize them. For Cumming the "control of the inanimate through universal mass action" is an epidemiologic fundamental in the control of any communicable disease.

Much has been written upon the danger of flies as a means of contamination and we, therefore, repeated the work of several observers and showed that flies fed upon tuberculous sputum were contaminated throughout with tubercle bacilli. They developed diarrhoea and the fly specks contained tubercle bacilli which caused tuberculosis when injected into guinea pigs. We then placed a receptacle of sputum containing many tubercle bacilli high up in a cage with guinea pigs and kept a dozen or more flies constantly in the cage, replacing them as they died. Specks found upon the carrots produced tuberculosis when injected into guinea pigs, but though we kept up the exposure for several weeks none of the guinea pigs developed tuberculosis. It is hardly probable that a child is often subjected to as much danger of contamination through flies as these guinea pigs were.

Infection through fomites, that is, contaminated objects, may in a few instances be the cause of infection in adults. I have in mind especially dressmakers who make over consumptives' apparel. The danger here, if the patient has undergone the present day treatment of living largely in the open, must be very slight for the reason I have already mentioned. In the laundry the danger is greater, particularly and chiefly with the handkerchiefs which are used at times, as everyone knows, as receptacles for infectious sputum. Boiling the laundry before handling it, or, better still, the replacement of handkerchiefs by gauze in all respiratory affections would abolish this danger. The gauze is, of course, burned after use.

Tubercle bacilli have been found in books used by consumptives but the danger must be so slight as to be negligible.

It has been suggested by Krause that children of three and four years of age, put to play on the streets, come in direct contact with tuberculous sputum. Their balls, tops, hoops, fall in the gutter or roll through masses of sputum on the sidewalks. Their infected hands quickly find their way to their mouth and tuberculous infection sooner or later results. It has occurred to me that a study of the sputum deposited upon the sidewalks and elsewhere might be made in a limited locality in Baltimore, and the children through the influence of the visiting nurse or by other means be subjected to the Pirquet test to determine what relationship, if any, might exist between the occurrence of sputum on the street and a positive skin test among the children.

I have mentioned what difficulties we have had in trying to find tubercle bacilli outside the body in a health resort and how our results for certain eating utensils were positive. It is interesting to note in regard to this that but one case of tuberculosis developed in any of the employees at the Trudeau Sanatorium during the thirty-six years of its existence. This case, one among many hundred employees, could easily have been contracted elsewhere and has never interfered with the woman's working ability. It was so slight that we might class it as doubtful.

The feces of all patients with tubercle bacilli in their sputum may be safely said to contain living tubercle bacilli. Whether they are excreted in the bile through the liver or come, as most probably do, from the swallowed sputum, is for our present purpose immaterial. The sewage of Saranac Lake empties into the Saranac River below the village. Mr. Petroff, Dr. Heise and I found tubercle bacilli at all levels of the river at the sewer's mouth but they grew less, as the mouth receded, to disappear at a distance of about four miles down the river, which flows about two to four miles an hour. It is hardly conceivable that under such conditions sewage contamination can play any important part in the production of tuberculosis.

To sum up our work, we have found tubercle bacilli on the eating utensils that are introduced into the mouth, on objects kissed, in particles of sputum coughed out, on the dust of floors on which patients have spat and in sewage. Gross contamination of hands, through wiping the lips or soiling with sputum, may be transferred to others, but has not yet been proved. It is not, of course, fair to draw too broad conclusions from a study of the habitat of consumptives trained in good hygiene and to apply it to the general population, where all rules of prophylaxis may be broken through ignorance or on account of weakness.

The virulence of the tubercle bacillus has been much dwelt upon by many writers. Largely irrespective of the number of bacilli, they say, the virulence may determine the type of disease. It is interesting to note, as Theobold Smith has pointed out, that very virulent tubercle bacilli may kill the infected individual so quickly that this strain of tubercle bacilli is destroyed, as it cannot escape from the body. On the other hand, a weakly virulent type may also fail to effect escape from the body, as no open disease is produced, and so remains imprisoned. These factors would tend in a broad way to equalize the virulence of tubercle bacilli in chronic pulmonary tuberculosis. But even a slight variation in virulence may be sufficient to make effective a superinfection, though it must be remembered that artificial reduction of virulence is due more often to reduction of the number of the living tubercle bacilli. I know of no one who has intentionally reduced the virulence of a tubercle bacillus and kept it reduced. The resistance of the host to the tubercle bacillus and the accidental location of disease has unquestionably more to do with the type of disease than variations in virulence.

Recently Brownlee has suggested that his studies lead him to believe that pulmonary tuberculosis is a mixture of several types of disease due to different strains or types of tubercle bacilli. It would appear that opportunities for infection, stress of life at different periods and evironment, are strongly complicating factors.

Three types of human tubercle bacilli have been separated by Petroff and it is possible that further knowledge may be gained by study of these and their correlation with the type of disease.

The number of bacilli on the other hand has a marked influence on disease. While a few may produce only infection or a slight superinfection, many may produce acute disease. Acute tuberculosis is often the result of an accident. A small area, a focus, of disease becomes crowded with tubercle bacilli and breaks into an artery or vein or lymph duct. An acute pulmonary or generalized tuberculosis may result. No one is so immune that a sufficiently large number of tubercle bacilli will not produce infection and ultimate disease.

Evidence can be adduced to prove that practically every possible, or impossible, method of infection that has been so far suggested, is not the usual one. Flügge had much difficulty in finding tubercle bacilli in the dust of streets or rooms and Cornet in turn attacked his droplet method, for coughing into the faces of animals does not seem to infect them with any degree of certainty, and yet 30 of 76 guinea pigs, kept in cages in wards with consumptives, became tuberculous. Bovine bacilli play some part in childhood infection but none in pulmonary tuberculosis in adults, unless we accept mutation, that is, that bovine can change into human tubercle bacilli, which no one has proved. Human bacilli may be carried from man to man by the slight infection imparted to them by the hands, but this seems unlikely, for we know that particles of dried sputum do not rub off easily and tubercle bacilli in thin layers are quickly killed by light and air. Hand-to-mouth infection is probably far more common than hitherto considered, and utensil-to-mouth infection cannot be ignored. Summing up the various methods of infection, it seems to me unwise to stress any one too heavily. Milk must be produced by nontuberculous cows or else pasteurized before use. Greater care must be given to the disposal of tuberculous sputum. The mouth must be covered with a piece of cloth during cough and stricter attention must be paid to rendering eating utensils, that approach the lips, sterile after use. From this the importance of strict hygienic measures for the patient with tubercle bacilli in his sputum, whether incipient or advanced, cannot be overemphasized. For the poor, hospitalization seems to offer the best means of preventing infection while the reporting of all cases is consequently of equal importance.

THE HOST

So far we have considered etiology from the standpoint of the tubercle bacillus. It is inconceivable that the host has no influence upon the development of disease, though upon primary infection it may exert little.

It is well known that children, healthy or weak, are nearly all susceptible to certain infections, for example, measles. To-day we are forced to believe that the same condition holds true for tuberculous infection; for, while possibly only 70 per cent of all individuals react to tuberculin at the age of puberty, thus proving that they harbor or have harbored tubercle bacilli in their bodies that have produced tubercles, several observers hold that all have a tuberculous infection before death while some affirm that this is so at the twentieth year. The movement of the people from the country to the cities, from where the population is sparse and relatively isolated to where it is dense, has certainly greatly facilitated infection, which some would have us believe is one of the true causes of the decrease in tuberculosis mortality. From this we may assume that, so far, all our methods of prevention have affected only massive infection, or have so raised the resistance of the more slightly infected that they hold their infection in a dormant state or, what is less likely, eradicate it.

This primary infection may occur with slight or indeed with no manifestations of ill health save a slight indisposition for a few days, though Pirquet believes that before the age of two years infection is usually manifested by some clinical symptoms, such as bronchitis. It is of interest to recall here how little influence a primary inoculation exerts upon the general health or at the site of injection in experimental tuberculosis. Stress has been laid upon what slight exposures are followed by primary infections in infants and young children. There can be no question that young children and primitive races, not hitherto exposed to tubercle bacilli, react very differently and much more acutely to infection with the tubercle bacillus than do those past puberty in the civilized races. The lymph nodes and tissues seem after the third year to offer a less favorable soil for the growth of tubercle bacilli. It is well recognized that the lungs also suffer at this age; but after puberty the lungs bear the brunt of the attack, and furnish what may be called the adult type of tuberculous disease which, however, can exist for years even when fairly extensive, and attract no attention.

Tubercle bacilli may enter the body (1) through the eyes, gaining access to the pharynx through the tear duct, (2) through the nose, and (3) through the mouth. Entrance through the skin can be disregarded for our present study. All three portals of entry converge in the pharynx and may lead to infection through the tonsils, as Crowe has shown, and through other masses of lymphoid tissue well distributed throughout the upper respiratory tract. Recent work has shown that inhaled bacteria can be recovered in the ultimate division of the lung, the air cells. Again, the tubercle bacilli may be swallowed and enter the body through the intestines which Calmette has recently emphasized and Theobald

Smith questioned. It would lead us too far afield to discuss here these modes of entry; but in an uninfected person the tubercle bacillus can pass through the slightly injured or normal mucous membranes, enter the lymph stream, pass into the blood and be filtered out in the small blood vessels and capillaries. They may lodge for a time in the case of the lungs in the lymph masses, but before long are transported to the lymph nodes about or near the roots of the lungs. Here they reach a final resting place and produce more or less tuberculosis. This area of disease, though it may be very small, is large enough to produce certain changes in all the cells of the body, which hereafter react to the tuberculin tests, though its effect upon the person may be so slight that he is hardly aware of it. His cells thus become sensitized to the tubercle bacillus, and when the latter again gains entry into the body or escapes from its primary site, it may be attacked more vigorously. It seems most likely that several portals of entry may be used at the same time or one after another by the different reinfections that are constantly occurring.

Chronic pulmonary tuberculosis is of extreme rarity in early childhood. In fact, some have held that a clinical diagnosis of tuberculosis during the first year of life spells death; but more recent figures show that even during the last three months of this year the prognosis is somewhat less fatal and that some resistance has been acquired. More deaths from tuberculosis occur during the first year of life than during any other (Hess) due, no doubt, to frequent reinfections with large doses of germs from tubercle bacilli carriers who fondle the babies. During the first two years of life the child is subjected usually only to the degree of infection present in the home and about 10 per cent are infected. If "home" infection is present it is possible that the infection may be severe and death more likely result. Even at this age the lungs rarely escape.

The bearing of these facts upon etiology is clearly evident. The infant and young child cannot be guarded too carefully against infections. In the household of the open case of pulmonary tuberculosis extreme care should be practised. If the mother has an open tuberculosis when the child is born it should be removed from home at once, and thus 97 per cent may escape infection, or else if at all possible kept apart from its mother. She should never nurse it. It is impossible, however, at this time to go further into the minute details necessary for the protection of young children in these households.

Up to the third year only 15 to 20 per cent have been infected. After this age, when the child begins to toddle about and make longer or shorter excursions into the outer world, opportunities for infection greatly increase, and infected toys, infected hands, infected spoons, as already described, may play a much larger part in primary infection than many have hitherto held. During the next four years, that is, from the third to the seventh year, 40 per cent of children are infected according to some statistics. Curiously, while the number of children infected increases with age up to puberty, the mortality decreases. If perchance a tubercle bacillus carrier, an open case of tuberculosis, is present in the house with a child under three years of age, infection takes place almost without exception, and tuberculous disease is much more likely to result from such extensive or repeated reinfections, though many still escape. Pearson has shown that the parent is twice as dangerous for the offspring as the tuberculous husband or wife is for the well member of the couple. This is another way of stating the fact that not only infection but disease is more likely to incur in those who are exposed early in life. However, Pollak found that after four years of age the entrance of a tuberculous patient into the family affected the child little, if at all; but, if introduced before this age, the child either grew up more delicate than its older brothers and sisters or if under two years of age was almost surely infected (96 per cent). Bergmann had no children die who were exposed after four years of age. In a study by Lampson 2 per cent of the family group without any tuberculosis gave a positive cutaneous tuberculin test, 22 per cent if latent tuberculosis was present, 67 per cent with open tuberculosis and 33 per cent with healed tuberculosis.

BOVINE INFECTION

When Detre announced (and by so doing is said to have won his bride) that individuals infected with bovine tubercle bacilli reacted more to tuberculin made from bovine tubercle bacilli than to that made from the human type, it was thought that a great step forward in the etiology of tuberculosis had been taken, but unfortunately no verification of this has been forthcoming. From the figures previously given it is seen how readily children might become infected by tuberculous milk when the exposure, though slight in amount, is so widespread. Krause has pointed out that the amount of childhood infection increases as soon as the child is able to walk, or in other words when he begins to play upon the street. He affirms that at this time the child drinks less cow's milk but it seems to me this is also the age at which less attention is paid to his milk, and it is also an age not so far removed from the time when he ceases to be breast fed. He has not excluded, it seems to me, the danger of infection by bovine tubercle bacilli, for many children consume much cow's milk from the age of three to seven. It is possible then that some of the infections that occur between these ages may be due to bovine tubercle bacilli. After puberty, bovine tubercle bacilli, which cause about 25 per cent of the disease up to this time, appear no longer able to produce much disease; for of a large series of cases investigated after this age, only 1.3 per cent had disease due to the bovine type and less than half of these were pulmonary disease. It is of interest to note that when all exposure to open tuberculosis can be excluded, 25 per cent of the children still react (Hillenberg, quoted by Roemer). Even inoculation of adults with virulent bovine tubercle bacilli seems to produce slight infection and apparently no disease. Many cases of tuberculosis of the glands of the neck, due to bovine tubercle bacilli, are either stationary or very slowly progressive. Some would explain such observations by stating that before the bovine germ is ingested, nearly everyone is infected and vaccinated with the human tubercle bacillus, a statement which is contrary to fact.

It appears impossible to-day to decide to which type of tubercle bacillus the majority of early infections are due. Into the homes where no carriers live the bovine tubercle bacilli come without doubt more frequently than the human type, but the youngster of three to seven years of age must have ample opportunity for infection while at play upon the street.

It would seem then a wise procedure to guard our children against tuberculous milk, and the provisions should be stricter the younger the child. For adults, unless the milk be very severely infected and undiluted with normal milk, the danger is negligible. The tuberculous cow should be excluded from all dairy herds but may be used for breeding purposes. It has been suggested that bovine infection protects against infection by the human type, and that it would be an unwise procedure to eradicate bovine tuberculosis. It has been advanced by Brownlee that his "middle age" type of pulmonary tuberculosis is closely associated with tuberculosis in children under five, and he implies that early tuberculosis in children, possibly bovine in origin, immunizes them against pulmonary tuberculosis in early adult life. But the resistance of the infected child may be at low ebb, the strain of the germ may be more virulent, the repeated doses may be massive, and so defeat our purpose. Instead of vaccination we may have to face disease. Such protection therefore is to-day too far from being proved to permit us to suffer a disease to continue to exist, which causes 10 per cent of all the deaths and at least 15 to 20 per cent of all the disease due to tuberculosis in children. It must be recalled, however, that tuberculosis is very common where bovine tuberculosis does not exist, and where cow's milk is never used for food. However this may be, I still hope that we may yet be able to inject a vaccine of bovine tubercle bacilli into man that will render him immune to human infection. Calmette claims that his strain of bovine tubercle bacilli, grown upon a potato medium, glycerinized and treated with ox bile, is not virulent for cattle and that in doses of at least 44,000 injected intravenously, it is nonvirulent for man.

HEREDITY

The tendency in tuberculosis work since the time of Villemin has been to emphasize infection more and more, and to belittle that unknown and mysterious factor, heredity. Some years ago Mr. Pope and I began a study of heredity but soon abandoned it as we saw no opportunity with the data at hand of arriving at any definite conclusion. That so called phase of heredity, the intrauterine infection of the child, is so rare, and the child succumbs so quickly that we need not consider it as of any practical importance. It is questionable how far, if at all, constitutional or hereditary factors prevent a first infection; but it seems to me that they may play a very important part in the development of disease from the primary infection or in the resistance to reinfection. For example, an ability to form tubercles may be entirely lacking as in white mice, or greatly lessened or indeed increased. Again the ability of the organism to react by the rapid and sufficient formation of fibrous tissue may be passed on in certain strains of the human organism. Tuberculoprotein hypersensitiveness can be inherited from a sensitive mother, but is inconstant and is probably never handed down to the third generation. The inheritance of certain physical peculiarities cannot be denied, and it is possible that after infection certain inherited characteristics may lead, on the one side to increased and, on the other, to lessened resistance and so to a less or greater tendency to frank disease. This has not been conclusively proved, though the work of Pearson and of Pearl is strongly suggestive. I can see no reason why certain families, if acquired characteristics can be transmitted to offspring, should not develop an ability to react with increased resistance, and King and Reibmayr affirm that children of tuberculous parents do. Under other conditions a liability to catarrh, or even to structural changes that favor infection may be inherited. Turban, Baldwin, and Strandgaard attempted to prove that pulmonary susceptibility was inherited in certain families in regard to point of origin of the disease in the lungs, its general course, and the age at onset. The small number of their observations do not lend them great weight.

The appeal to medical work published before the discovery of the tubercle bacillus as some (Bullock and Greenwood, and Bushnell) have done, does not bear much weight, for many of the predisposed, with fair, white skin, flushed cheeks, soft and slender muscles, have probably already been infected, and their development in some way arrested. Here the tubercle bacillus may be or is the cause of the predisposition.

The inheritance of predisposition to pulmonary tuberculosis is, Pearson and others affirm, just as likely to occur as the transmission of normal physical characteristics or as insanity and deafmutism. The relationship between husband and wife in regard to pulmonary tuberculosis is far less close, and so indicates that infection is not the chief factor, for where selection of mates is freer, for example, among the middle classes, the relationship is closer than among the poor. Infection and acquired resistance, as Cummins has pointed out would, however, explain this as well as heredity.

Race has unquestionably some relationship to the mortality from pulmonary tuberculosis. It has been found that more children among the Italians than among the Irish react to tuberculin but more Irish than Italian adults die from pulmonary tuberculosis. Here again racial temperament and infection complicate the study. Apparently savage races, as well as negroes and American Indians, show a lessened resistance to pulmonary tuberculosis.

The whole question is greatly complicated by the fact that slight early infection increases resistance to the tubercle bacillus, and some would affirm that this is the more plausible assumption (Cummins). The reaction to the tubercle bacillus of savage tribes who have never come in contact with the tubercle bacillus is no argument against a tuberculous diathesis, for, as Pearson has pointed out, such races may include many families with less natural resistance to the tubercle bacillus than others. Then again lack of all hygienic conditions makes massive infection from a tubercle bacillus carrier the rule.

If the host can react to the tubercle bacillus, it is also possible for the parasite to react to the host, as Dr. Welch pointed out in his Huxley lecture in 1902. The whole theory of exotoxins, that is, poisons given off from the living germ, is associated with the reaction of the parasite to the host. Another point of interest is the question whether such a reaction may lead to greater powers of resistance on the part of the germ, and so enable it to repel better the attack of the same strain of tissue. I mean by this that a tubercle bacillus which has successfully overcome the resistance of one offspring may prove of greater danger to another offspring of the same father and mother than one not so related. Parental infection, according to this, would not be as dangerous as infection of offspring by offspring. There are no data on which to base this assumption, and accordingly no especial reason to forbid members of a family from nursing one another.

In any case the question is not, as Pearl says, whether all disease is due to constitutional factors alone or to environment alone but how much influence does each factor exert in the development of the disease. The question is still unsettled, and I hope that Pearl's work now under way will help much to clear this vexatious problem.

SUPERADDED INFECTION

Reference has been made to reinfections in the same individuals, and here again we are much at odds. Several years ago Behring stated that all tuberculosis was due to bovine infection, which was acquired early in life, remained latent during childhood, and only later in life developed from infection to disease. Much work has disproved this. A well known worker in tuberculosis wrote some years ago, "Childhood is the time of infection, youth the time of superinfection, and that from extension of the primary disease." This would of course exclude adult reinfection, and would render any man or woman with a positive tuberculin reaction ordinarily immune to tuberculosis. The importance of these views in the antituberculosis campaign is very evident. Only individuals who have been infected should engage in tuberculosis work for they, it would imply, are safe from further infection but, on the other hand, just as liable as others to the development of disease from the primary infection. In fact, any one who reacted to tuberculin could pay little heed to further infection from without but much to the avoidance of debilitating circumstances.

THERE IS NO REINFECTION FROM WITHOUT

Many arguments have been advanced to show that adult reinfection rarely, if ever, occurs, and that pulmonary tuberculosis is the development of childhood infection. We have said that 70 per cent of individuals have had tuberculosis in their bodies by the age of puberty, and some affirm that all are infected by the age of thirty. Infection occurs much more easily in early life. Apparently normal lymph nodes may contain living tubercle bacilli which are found at times even in completely calcified areas of former disease. Pulmonary tuberculosis follows more often depressing influences than any recent exposure to infection. Close association in adult life causes apparently little increase in mortality of those so exposed. The fact that the lungs are chiefly affected in adult life may be due to the fact that injuries are less frequent than in childhood, and that the lungs are the great filter for any germs that escape into the circulation.

Some have suggested that reinfection from without is less likely to occur when the resistance is lowered; for the tubercle bacilli in the body have already adapted themselves to the host and consequently the usual reinfection would be from within. If the tubercle bacilli can adapt themselves to the host, it is also possible for the host to develop greater powers of resistance against this primary strain. Such reasoning is of course hypothetical, and Roemer could detect no difference in reaction in guinea pigs by inoculation of the skin. Infection from within is clearly the most common method of progression of the disease in experimental tuberculosis and of its spread to the lung, though reinfection from heavily contaminated feces and urine may be conceived. Roemer himself showed that only when very small doses were employed did animals fail to become superinfected, and not only the number but the virulence may overcome this resistance in man.

Tubercle bacilli unquestionably long lie dormant in tissues apparently normal, though some claim more careful study would reveal microscopic disease; but it is difficult to see why doses sufficient to produce disease later in life, which some hold must be "massive," do not produce disease at the time of infection early in life when the body is more susceptible to the tubercle bacillus.

In a recent important and timely book Bushnell has attempted to show that only massive infecting doses, such as very rarely if ever occur in the life of man, can cause a reinfection from without. He assumes that every individual who harbors tubercle bacilli may excrete them at times through his intestine. He also assumes that the vaccination from childhood infection persists throughout life, which we know is not true for calves and cattle. Tubercle bacilli which escape into the blood stream, he says, cause no new areas of disease. He quotes the experience of Lippspringe, where, with enormous numbers of consumptives (8,000 per year in 1906–1909), crowded into narrow quarters with the natives, taking no special care of the sputum for many years, the tuberculosis mortality fell from 98 per 10,000 in 1831–1840 to 35 in 1906–1909. The population was 1440 in 1830, and 3472 in 1909. So, he argues, quoting Werner, that the contagionist's view as to the high infectiousness of pulmonary tuberculosis is false. In Schlanger the same was true. It is of some interest to recall that for ten years no native in Saranac Lake (population about 5000) died from pulmonary tuberculosis, and the high death rate quoted in these two health resorts appears to suggest that either the death rate among children was excessive, or that the bad hygienic conditions fanned childhood infection into adult disease or that adults were reinfected. The argument is advanced that patients with malaria or syphilis are immune to further infections, and so by analogy a second reinfection with tubercle bacilli is not possible. This assumes that tubercle bacilli once in the body never die, for if syphilis be cured a second infection readily takes place. That the tubercle bacillus never dies has not been shown, and cattle experiments controvert this view. According to this view, the worst thing that could happen to a patient with pulmonary tuberculosis would be to recover entirely.

Some years ago Mr. Pope and I attempted to prove infection. We collected 40,000 married couples, one of whom was tuberculous, both of whom were dead, and so, by excluding any connecting hereditary taint, hoped to arrive at some estimate of the danger of infection from husband to wife or vice versa. But even here "assortative mating," that is, that persons with the same physical and mental tendencies are more likely to marry, enters and complicates the situation. There was definite evidence of infection but two-thirds of this was thought by Pope and Karl Pearson to be due to assortative mating. If one wishes to deny this influence there is definite evidence of infection, though not great, of one consort by another. Most of the recent statistics on this fact are of small value as one, the healthy, or often both, of the parents are still alive. Though here too another difficulty enters, for some of the well spouses may develop tuberculous disease, and recover from it, only to die of nontuberculous disease.

Attention has been drawn by Hess to the fact that deaths from all forms of pulmonary tuberculosis increase very markedly at thirteen in girls and at sixteen in boys or, in other words, at puberty, which he thinks is the determining cause of this increase. He then states that if this is due to infection, such infection must have been continuous, which he disbelieves though he refers to "tubercle bacilli shedders." He advances this as an argument against reinfection from without and in favor of reinfection from within. It could also be used as a demonstration of change or decrease of immunity at puberty which favors reimplantation of tubercle bacilli from without.

Newsholme has pointed out that figures quoted from hospitals for the tuberculous when carefully analyzed may show that reinfection has occurred. The same holds for other figures (Freymuth).

REINFECTION FROM WITHOUT OCCURS

On the other side are many facts that suggest that reinfection from without may play a very important part in many cases. Krause has shown experimentally that a primary infection by the vein in guinea pigs leads to the temporary presence of tubercle bacilli in the lungs. A second infection by inhalation produces a very different picture for here the tubercle bacilli are "fixed" in the lungs which react severely, and in certain immune animals the tubercle bacilli are destroyed apparently in time. In those individuals who have lost in large part their immunity or in whom the dosage is too large, no such retrogression occurs, and infection is followed at once by disease.

It is also of interest to recall that Winternitz, from a study of poisonous gases, is led to conclude that the portal of entry of bacteria into the lungs is through the air currents which may finally deposit the germs in the ultimate recesses of the lungs. It has long been known that of all natural methods of infection, that by inhalation requires the smallest dose. Even avirulent tubercle bacilli, when sprayed into the faces of guinea pigs, cause the formation of tubercle in the lungs, tubercles however, which may ultimately disappear. This, of course, would explain what happens to many pulmonary infections in adults. It is also very suggestive that reinfections of guinea pigs by the vein does not lead to such a marked formation of pulmonary tubercles. The experiments that show that reinfections can occur in animals are numerous. In fact, Roemer, one of the great opponents to reinfection, had to use very minute doses of tubercle bacilli or he would reinfect his animals. In some experimental work certain bacteria caused pneumonia only when sprayed into the air passages, and not when inoculated. It is of interest also to note that it is very difficult to infect rats by inoculation but comparatively easy to do so by the aerial route. We must bear in mind the fact that a primary infection by a moderate number of tubercle bacilli leads to involvement of the nearest (regional) lymph glands, while a secondary infection does not involve these glands. The work of Opie has convinced him that two types of tuberculous lesions exist in the lungs, one occurring anywhere in the lungs, not fatal, but often healed, and associated with involvement of the lymph glands; the other in the apex of the lung, often fatal, and not associated with involvement of the lymph nodes. The latter, he holds, is modified by the primary infection, though due to a slight infection which he implies, I take it, is from without.

From figures collected by the Imperial German Bureau of Health, in a study of 1400 cases with reference to the occurrence of human and bovine tubercle bacilli, it was found that 50 per cent of the tuberculosis of the abdominal lymph nodes, 41 per cent of the lymph nodes of the neck, 23 per cent of general tuberculosis, and no cases of pulmonary tuberculosis where due to the bovine bacillus in children, where the infection is almost certainly due to imbibed milk. Adult pulmonary tuberculosis is due to the human type in 99.3 per cent of all cases, where the disease is manifest, and it is of interest to compare these figures with those where the infection is known to be by ingestion. It implies to me that infection through the respiratory tract is often the cause of pulmonary tuberculosis, and that possibly in a larger number of cases than many would like to admit the cause of pulmonary tuberculosis is direct infection of the lung. Opie's recent work on British and American soldiers would suggest that infection (or reinfection?) by ingestion might preclude pulmonary disease.

Ward in a study of rural tuberculosis in England comes to the conclusion that adult infection does occur. In 252 cases, he attributed 40 per cent to immediate infection, 19 per cent to remote, 10 per cent had only a doubtful contact and 31 per cent no discoverable contact. In 96 children, 74 per cent were immediate, 2 per cent remote, 1 per cent doubtful and 23 per cent negative. He investigated 102 nontuberculous control cases and found 5 per cent exposed to immediate, 7 per cent to remote infection, 6 per cent to doubtful, and 82 per cent to none. A study of 77 tuberculous soldiers showed 5 per cent immediate, 26 per cent remote, 2 per cent doubtful and 67 per cent negative exposure.

The argument, that never in adult life is the infecting dose of tubercle bacilli large enough to bring about reinfection and disease, can be opposed by the statement that a series of reinfections, each of which is small in itself, may aggregate in the whole a fairly large dose. None deny that massive infection from without can produce disease in adult life. Some who deny reinfection emphasize the importance of tubercle bacillus shedders, which they say, play a large part in primary infection, but none, they imply, as sources of reinfection. Another interesting fact is that adult pulmonary tuberculosis is almost always situated at the periphery where inhalation infection would explain it, while childhood infection most often arises around the roots of the lungs. In the cases whose tubercle bacilli in the primary infection are well walled off, debilitating conditions can be supposed to arise which might lead such foci to act like loci minoris resistentiae for a superinfection from without, while still preventing infection from within. The whole thing seems to be a matter of the balance of resistance and dose and possibly virulence.

The experience with immunity in cattle is of interest in this connection. Without going into detail, it may be recalled that calves can be immunized by the injection of human tubercle bacilli, and when placed in a cow barn with tuberculous cows remain well for many months; but after two years many, if not most, of them develop pulmonary tuberculosis due to the bovine germ. Either one of two things has happened; first, the human tubercle bacillus has been changed into the bovine or, second, a secondary infection has taken place from without, and disease has resulted. The transformation of one type of tubercle bacillus into another has never been observed and we are forced to accept the latter explanation. Calmette's recent work with bovine tubercle bacilli has also upheld this conclusion.

Deaths from tuberculosis occur least frequently between the ages of ten and fifteen. From this time on the mortality from tuberculosis increases, and the lungs are the organs most frequently attacked. After this age the bovine infection, which was fairly frequent before, now becomes, so far as the lungs are concerned, almost negligible. Previous reference has been made to the possible changes that occur in the body at this time and their possible bearing upon the bovine tubercle bacillus. It has seemed to me possible that many of the tuberculin reactions in the skin that occur early in life may be due to infection by the bovine tubercle bacillus for the reasons already mentioned. About puberty many of these infections probably become quiescent or die out entirely.

In fact, bovine tubercle bacilli, virulent for rabbits, have been inoculated subcutaneously into men, some of whom were tuberculous, but in none of the fourteen instances did anything more than a local abscess ever develop. Bovine tubercle bacilli are more susceptible to light and drying than human. It is also conceivable that infection by greatly weakened tubercle bacilli may bring about immunity, though in time they also may gradually weaken and die. From this time on the immunity which has apparently existed from the eighth or ninth to the fifteenth or sixteenth years begins to decrease, and from the twentieth to the thirtieth years the decrease is very marked, if increase of mortality is an indication.

Personally, I do not believe that all the immunity reactions are lost; for I believe that cellular immunity outlasts by far any of the humoral indications that we have. It seems to me that we must in our intercourse with the world come in frequent contact with the human tubercle bacillus, and as we grow older it is probable that infected objects play a smaller part in our reinfections. Inhalation infection requires far fewer tubercle bacilli than ingestion, and it seems to me possible that sooner or later all of us breathe tubercle bacilli into our lungs. Where the cellular immunity persists the tubercle bacilli are probably attacked and localized in the first mass of lymph cells they reach. I do not believe that many of these infections "take," that is, develop into disease, but sooner or later some do, and the resulting pulmonary tuberculosis is due to this secondary infection occurring from without in adult life. This does not mean that the reinfection may not lie dormant for a long time, for in many instances I believe it does. Nor would I deny that tubercle bacilli entering the body through the upper respiratory tract or elsewhere may not reach the lymph vessels, and passing through the blood find a lodging place in the lungs, there to act similarly to those inhaled. I am inclined to believe that 50 per cent of all adult pulmonary tuberculosis is due to reinfection after puberty. Reinfection is probably less frequent after the third decade. For these reasons it seems to me that the care of the patient with advanced pulmonary tuberculosis is very important in the eradication of adult pulmonary tuberculosis on account of this danger of superinfection.

FACTORS THAT FAN INFECTION INTO DISEASE

That reinfection can occur from within cannot be denied. Complications arise in organs not exposed to direct infection from without. Clinical relapses occur and the areas of disease spread both to the same and to the opposite lung. Symptoms arise for the first time in disease of the lung which both physical signs and X-ray plates show is of long standing. Trauma also causes apparently new localizations of the tubercle bacilli and tuberculous disease which did not previously exist, but affects pulmonary tuberculosis but little. The strain of pregnancy lights up not only known disease but brings to light unsuspected disease in women hitherto apparently healthy. Measles acts in a similar way, and some hold the same is true for the common colds and influenza. Whether pulmonary tuberculosis results from reinfection from within from a primary childhood infection or from an adult reinfection from without, it is probable that more or less time elapses between reinfection and clinical disease. This latent period may vary from a few weeks to many years; for it is a question how soon, if ever, some tuberculous infections die out. (Some hold that even acute tuberculosis is always due to reinfection.) The fact that the vast majority of all adults have been infected, have been able to hold the pathological changes thus produced in abeyance, indicates that they have some resistance, and it therefore becomes very important—I cannot stress it too much if all of us become infected—to know what untoward circumstances upset the balance in favor of the body and turn the scale to favor the germ.

The development of infection into definite clinical pulmonary tuberculosis may be due to any debilitating circumstance. Recently, it has been pointed out that lack of sufficient food has increased the mortality from tuberculosis in Germany, until it has risen to what it was twenty to thirty years ago. It would appear from this that increased wages which would provide better food would also decrease the amount of pulmonary disease and the number of cases that die from it. Too little use of milk as a food is also an important factor.

Dusty trades have been much studied recently, and some have come to the conclusion that only certain dusts are of much importance, depending upon the character of the individual particles, and upon the chemical composition. Sharp, angular particles of dust, metallic or mineral dust, are much more dangerous than street or organic dusts. Gardner has found tubercle bacilli more frequently in the lungs of guinea pigs which had inhaled granite dust than in the controls, but the "dusted" animals had a longer life. Colds are a frequent precedent of the development of clinical pulmonary tuberculosis, and it has been suggested that adsorption of certain antitryptic ferments by the bacteria circulating in the blood during these infections might bring about this condition. Measles and influenza affect for a time the sensitiveness of the body, and some think in this way favor the spread of infection into disease. Repeated pregnancies and lactation are held to do the same thing, not only for cows, but for women as well. Indeed a single pregnancy at times appears to cause clinical pulmonary tuberculosis. Diabetes also predisposes to clinical disease.

In another large class fall all those conditions that we feel prevent the recovery of patients with pulmonary tuberculosis. These may act to change quiescent infection into active pulmonary disease. Change from an outdoor to an indoor life is bringing down many of our boys who fought in the war. Severe physical exertion acts only when the thread of resistance is nearly broken. Poor housing, insanity, dirty quarters, may also favor infection from without, but Todd, who has studied the situation in Chicago, feels it is difficult to prove by statistics the direct relation between tuberculosis and house. Chicago, he believes, contains more small bedrooms than any other city. The Italian blocks have more opportunity for crowding in small bedrooms but less crowding occurs than in Polish blocks, and yet have more tuberculosis. Curiously he finds more tuberculosis in blocks where children are fewest. The economic environment in the house, the use made of the house, and other factors, not as yet studied, for example, the history of the occupants of a single house over a term of years, all enter into and disturb any conclusions. Hence the term "house disease" must be applied to tuberculosis with caution. I would refer any one interested in this subject to the bibliography compiled by James Ford (*American Journal of Public Health, vol. x, 1326*).

Pulmonary tuberculosis is closely connected with the general death rate, and often rises and falls as it does. Poor general sanitation, particularly where bad water supply favors intestinal diseases like typhoid fever or where intestinal parasites are frequently found, all produce apparently more pulmonary tuberculosis.

It must not be forgotten finally that inability to take needed rest, too long hours of work, particularly in poorly ventilated rooms, inability to relax or to play, or again too hard play after long hours of work, burning the candle at both ends, all cause pulmonary tuberculosis to spread in extent and can fan into existence an all but eradicated infection.

The whole subject of the etiology of pulmonary tuberculosis is still far from settled. I shall offer no conclusions to what I have said. All of us have our eyes fastened on this school of hygiene, hoping it will lead us into newer, clearer conceptions of the causes of pulmonary tuberculosis, and so enable us to bring about a great reduction of this disease, which to-day takes so large a toll of mankind at its period of greatest efficiency.

THE EFFECTS OF LIMITING THE RESPIRATORY EXCURSIONS OF THE UPPER THORAX IN REFRACTORY CASES OF PULMONARY TUBERCULOSIS

A PRELIMINARY REPORT

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Of all the procedures that have been applied to the control of the toxic symptoms of pulmonary tuberculosis none can be compared for dramatic effectiveness to the induction of artificial pneumothorax.

Curiously enough, the literature is nearly silent on the final results of this treatment; nevertheless, the near phenomena of amelioration are so striking that we may be justified in assuming that collapse of the diseased lung through the introduction of air into the pleural cavity involves at least some of the essential factors in the cure of tuberculosis. It is by no means self-evident as to how such pulmonary collapse accomplishes symptomatic improvement. Could we be sure of the details of the process there would be established, in general consent, a rational scheme of treatment.

We have now and then asked experienced clinicians their views as to just *how* artificial pneumothorax helps in the treatment of tuberculosis. The answers were delphic in their ambiguity; they explained everything and nothing.

Without dwelling longer on this theoretical, if highly important, theme, we will venture to state explicitly certain views as to the rationale of pneumothorax therapy. We assume (1) that the prime effect of pulmonary collapse is reduction in the amount of toxins given over from the diseased lung to the general circulation. We assume (2) that the chief agency in the dissemination of toxins is the respiratory movement of the lung; that, by means of its excursions the lung acts as a veritable pump for the distribution of its liquid contents; that, given an intrapulmonary reservoir of poison open to the general circulation, its contents will be mobilized with a rate proportionate to the amplitude and rapidity of respiratory movement.

We claim no originality for these views, but only that they are clear.

We purposely hazard no guess as to what changes are induced in the lung on the side opposite to that of pulmonary collapse. One of us has ventured, in another place, to approach this subject (1). If the propositions announced above be admitted, it follows that the distribution of toxins from a diseased pulmonary focus will be brought to its minimum by inhibiting motion of the part. It is a demonstrable fact that the lungs in their respiratory movements rather strictly follow the local excursions of the adjacent overlying thoracic parietes. When respiratory movement is limited to the diaphragm it is the very bases of the lungs that move most widely, the extent of motion rapidly diminishing upwards. When the upper chest expands, respiratory motion involves the upper lobes in proportion to the excursion of the overlying ribs. Now, it is familiar enough that, broadly speaking, pulmonary tuberculosis is a disease of the upper part of the lungs, its intensity being concentrated between the hilum and the extreme apex.

Remembering the data of our argument, the deduction is obvious that were we able to inhibit respiratory motion in, say, the first four ribs we could, without seriously imparing the vital capacity of the chest, so restrict the motion of the principal areas of pulmonary disease that distribution of the toxins therefrom would be greatly reduced. Every medical student is familiar with the therapeutic uses of strapping the chest. In fact, a Colorado medical pioneer, the late Charles Denison, probably left little to be accomplished in this regard beyond his ingenious devices for unilateral immobilization of the chest (2). As may have been anticipated, our own scheme for fixing the upper ribs has to do with an encircling band which must symmetrically restrain inspiratory movement of the upper ribs of each side. We are aware that this method has been applied before, but we can find no definite description of the procedure and its purpose.

We would not have felt justified in applying our treatment, at the outset at least, to the ordinary case of pulmonary tuberculosis. We have used it for the reduction of toxemia only in such patients as still showed fever or toxic symptoms after prolonged bed rest, such as would usually fit the subjects for active exercise. Two distinct classes of cases fall within this category; the first consists of persons who, without marked signs of tissue disintegration, are evidently hypersusceptible to tubercularization; the second class is composed of that great group of "third-stagers," whom by common consent we try to make comfortable while they live and render as harmless as possible until they die. We have not even applied the method within this group to cases that would seem to admit of the artificial pneumothorax. Our cases were, on the whole, such as seemed unamenable to other therapeutic aid.

Among the approximately 170 patients at the National Jewish Hospital for Consumptives at Denver there is always a large contingent of invalids far advanced in disease. The great majority are of Jewish stock and are peculiarly temperamental. The present nursing facilities of the hospital do not admit of general absolute bed rest for inmates. Except when acutely ill, patients visit the bathrooms for washing and toilet purposes, walking a distance of 40 to 60 yards for the purpose. Moreover, they commonly sit up for meals at bedside tables. Under these conditions it may be believed, it is common to find patients running an irregular and elevated temperature and with various signs of toxemia month after month.

Dr. Swezey, Medical Superintendent of the hospital, selected half a dozen especially refractory cases for treatment by the plan described. It should be said that care was taken to change in no particular the treatment of the selected patients, except to restrict the motion of the upper ribs.

Our first experiments were made by encircling the chest, for a width of some three inches, with overlapping strips of adhesive plaster, applied while the patient held his breath in expiration, the upper level of the strips reaching high into the axillæ. For obvious reasons, the adhesive plaster was applied not directly to the skin, but over a light bandage.

Injury to the axillary folds was avoided by local padding with absorbent cotton. Later it was considered preferable to substitute for the plaster simple belts made of dressmakers' belting, known to the trade as "herring-bone belting." Strips of this material, 3 to 3½ inches wide, were cut long enough to overlap some 5 inches when encircling the chest. To one end of the belt three buckles were stitched; and corresponding strips of webbing, such as is used in suspender garter straps, were sewn to the belt about 5 inches from the other end. It may be clear that the belt so constructed can be buckled tightly around the chest with an adjustable range of several inches. Belts of different lengths must, of course, be provided to fit various girths of chest. We have found a range of 26 to 33 inches in length to suffice for all the paients with whom we have dealt. With materials at hand, an average worker can, on the sewing machine, put one of these belts together in ten minutes.

As, in spite of its tight stricture, a belt often tends to slip down, it was held in place by a narrow shoulder strap running through loops, one at the back and two in front, on the belt and fastened, like the latter, by a buckle. Careful padding of the axillae was necessary to prevent abrasion of the skin. Patience and care seldom failed to make the wearing of the belts tolerable if not indifferent to the invalid.

The patient was instructed that the sole object of the belt was to inhibit motion of the upper chest and restrict respiratory movement to the diaphragm and that the belt could be loosened as these purposes were accomplished. Some patients, women especially, could not sleep comfortably in the belts at first; in which event the girdle was loosened or removed at night. In practically all cases, however, the belt in time was worn continuously without complaint. So obvious was the advantage of the procedure in certain cases that after it had been in operation some weeks patients began to volunteer requests to be treated with the appliance.

As will be seen from the detailed reports of the cases, there was a general improvement in the range of body temperature, but what cannot be portrayed was the frequently marked symptomatic improvement manifested in the elimination of the evidences of intoxication. An interesting objective sign of the operation of the method on the diseased lungs is given by comparing the skiagrams of the chest taken before and after a course of treatment. The second group of plates shows a somewhat uniform increase in the density of the shadows which we ascribe to the establishment of healing fibrosis. Unfortunately these details are not such as easily lend themselves to graphic reproduction.

Up to the date of writing, April 15, 1921, eighteen patients have been treated at the hospital for various periods. The following is a brief summary of the results: The cases reported include only those that had or have worn the belt more or less continuously from eighteen days to five months. These are 18 in number. Three cases grew worse; 2 cases were not materially changed; 13 cases improved. A case (3794) that was possibly injured by the belt was that of a young woman who was about to be dismissed as hopeless. Besides extreme pulmonary involvement there was shown by X-ray a large filling defect, probably tuberculous, in the transverse colon. For ten days or more after application of the belt, her temperature and other symptoms abated markedly, but then the abdominal disorder became more obtrusive and the belt was removed. We concluded that a prominent contraindication to restriction of costal respiration is found in tuberculous lesions below the diaphragm because, of course, the increased abdominal motion contravenes in this area that rest for active foci which theory demands.

In 2 of the 18 cases, no essential change in the clinical condition could be detected as a result of the treatment. Eight patients somewhat more than held their own during treatment, and these are recorded as "improved." Four patients were "much improved." One patient was "very much improved." It was a common experience to witness a sharp rise in the temperature curve on the day when the belt was removed and a subsidence of the fever when the pressure was resumed.

Considering the class of patients included in the above summary, these results are encouraging and we are inclined to believe that the method as illustrated, or some modification of it, offers to the clinician a new technical procedure of value. Bearing in mind that the theory on which restriction of costal movement is advised assumes that the poison-producing foci are essentially aggregated within the zone of compression by the belt, it is obvious that when active lesions are seated in the inferior half of the lungs, or below the diaphragm, as in the case recorded above, we should expect that compression of the upper chest would do harm rather than good.

Certain of our patients have worn their belts more or less continuously for over five months with rather general improvement in their clinical condition. We are inclined to advise, however, that in most cases the application of the belt be made a temporary resort and combined with bed rest, and that the stricture be removed when the body temperature has remained normal for several days. This is but a preliminary report and the device described has not yet been applied during hot summer weather.

CASE REPORTS

No. 3664. B. A. Male. Age thirty-five. Admitted May 16, 1919. Duration of disease about two years. *Extent:* Far advanced pulmonary tuberculosis. Marked involvement scattered throughout both lungs, especially on left. Large cavity in upper left. Also chronic tuberculous laryngitis. Chronic nephritis. *Character of symptoms:* Almost constant headaches. Frequent attacks of dizziness. Rapid loss of weight and strength. Cough and expectoration. Fever up to 101°. Belt applied November 5, 1920. Belt worn to date, April 15, 1921. *Change in symptoms and signs following application of belt:* No objective signs of improvement. Patient, however, claims he is feeling better and insists on wearing the belt. *Condition unchanged.*

No. 3708. M. P. Male. Age thirty. Admitted July 18, 1919. Duration of disease about three years. *Extent:* Far advanced pulmonary tuberculosis. Extensive involvement throughout both lungs especially on right. Large cavity in upper right. *Character of symptoms:* Severe cough and expectoration. Fever up to 101°. Weakness, dyspnoea. Belt applied November 8, 1920. Belt worn to date. *Change in symptoms and signs following application of belt:* Temperature somewhat lowered. Cough and expectoration slightly improved. *Condition slightly improved.*

No. 3794. L. K. Female. Age twenty-two. Admitted January 30, 1920. Duration of disease about two and a half years. *Extent:* Advanced pulmonary tuberculosis. Marked involvement throughout both sides with considerable consolidation and fibrosis. Cavity formation in upper left. Tuberculous enteritis. *Character of symptoms:* Very severe cough and expectoration. Average temperature variation, 97° — 101°. Extreme weakness. Headaches. Abdominal distress. Belt applied October 28, 1920. Belt worn until December 4, 1920. *Change in symptoms and signs following application of belt:* Probably aggravated abdominal condition. Abdominal pains and distress more frequent and more marked. *Condition worse.*

No. 3816. J. C. Male. Age eighteen. Admitted March 21, 1920. Duration of disease about two years. *Extent:* Advanced pulmonary tuberculosis. Some involvement scattered through both lungs. Probable cavity in upper left. *Character of symptoms:* Occasional fever up to 99.5°. Lack of appetite. Cough and expectoration. Weakness. Loss of weight. Belt applied March 11, 1921. Belt worn to date. *Change in symptoms and signs following application of belt:* Cough, expectoration and appetite slightly improved. Feeling better. Temperature normal. *Condition slightly improved.*

No. 3819. C. K. Female. Age twenty-one. Admitted March 25, 1920. Duration of disease about two years. *Extent:* Moderately advanced pulmonary tuberculosis. Some involvement in upper right. Considerable fibrosis and glandular changes in both hila. Considerable involvement scattered throughout both lungs. *Character of symptoms:* Fever up to 100. Loss of weight, weakness. Cough and expectoration. Artificial pneumothorax tried first on right: no results (adhesions). Then tried on left: no results. Belt applied March 7, 1921. Belt worn until March 25, 1921. *Condition unchanged.*

No. 3829. L. G. Male. Age twenty-seven. Admitted April 23, 1920. Duration of disease about two years. *Extent:* Advanced pulmonary tuberculosis. Considerable involvement of both uppers, especially the left. Considerable inflammatory mottling throughout both bases. *Character of symptoms:* Lack of appetite, tired feeling. Slight loss of weight. Cough and expectoration. Belt applied February 28, 1921. Belt worn to date. *Change in symptoms and signs following application of belt:* Slight gain in weight. Appetite improved. Cough and expectoration greatly improved. Feels stronger, has more "pep." *Condition improved.*

No. 3836. I. H. Male. Age twenty-seven. Admitted May 5, 1920. Duration of disease about one year. *Extent:* Considerable involvement of upper left. Some scattered throughout lower left. Peribronchial thickening. Tuberculous otitis media on left. *Character of symptoms:* Maximum temperature frequently up to 100°. Weakness, lack of appetite, cough and expectoration. Extreme nervousness. Belt applied February 28, 1921. Belt worn to date. *Change in symptoms and signs following application of belt:* Temperature down to normal. Cough and expectoration greatly improved. Appetite better. Nervousness greatly relieved. *Condition much improved.*

No. 3850. S. F. Male. Age thirty-one. Admitted May 29, 1920. Duration of disease about two years. *Extent:* Far advanced pulmonary tuberculosis, with cavity formation in upper left. Considerable involvement scattered throughout both lungs. Chronic laryngitis. *Character of symptoms:* Severe cough and expectoration, extreme weakness, loss of weight. Anemia. Temperature up to 101°. Confined to bed. Hemorrhage, August 4, 1920, two ounces. Belt applied November 2, 1920. Belt worn two months and three days. *Change in symptoms and signs following application of belt:* Markedly improved.

Great diminution of cough and expectoration. Perfectly healthy complexion. Temperature, pulse and respiration normal. Gained about twenty-five pounds. *Condition very much improved.*

No. 3872. L. S. Male. Age twenty-eight. Admitted July 11, 1920. Duration of disease about two years. *Extent:* Advanced pulmonary tuberculosis with marked involvement throughout both lungs. Cavity formation in upper left. *Character of symptoms:* Severe cough and expectoration, temperature 103°, pulse 140. Loss of weight, extreme weakness, night sweats, extreme nervousness. Belt applied October 31, 1920. Belt worn to date. *Change in symptoms and signs following application of belt:* Great diminution in cough and expectoration. Temperature came down to 99°—100°. Gained weight. *Condition improved.*

No. 3883. H. D. Male. Age thirty-one. Admitted July 29, 1920. Duration of disease about five years. *Extent:* Far advanced pulmonary tuberculosis with marked involvement throughout both lungs. Pleuritic thickening and fibrosis in upper right. Shifting of mediastinum to right. Multiple cavity formation in upper right. Small cavity formation in upper left. *Character of symptoms:* Loss of weight, weakness, slight fever up to 100°, streaked sputum, considerable cough and expectoration. Confined to bed. Belt applied November 11, 1920. Belt worn to date. *Change in symptoms and signs following application of belt:* Marked diminution in cough and expectoration. Temperature, pulse and respiration normal. *Condition much improved.*

No. 3884. D. C. Male. Age forty-nine. Admitted July 29, 1920. Duration of disease about two years. *Extent:* Far advanced pulmonary tuberculosis. Marked involvement throughout both lungs, especially uppers. Considerable fibrosis. Cavity formation in upper right. *Character of symptoms:* Severe cough and expectoration. Extreme weakness, loss of weight, loss of appetite. Temperature variations 97°—101°. Hemoptyses. Confined to bed. Belt applied November 13, 1920. Belt worn until February 15, 1921. *Condition worse.*

No. 3907. A. S. Male. Age twenty-seven. Admitted September 6, 1920. Duration of disease about one and a half years. *Extent:* Far advanced pulmonary tuberculosis. Marked involvement in both lungs, especially the left. Annular shadows in both uppers. Tuberculous laryngitis. *Character of symptoms:* Very severe cough and expectoration. Belt applied January 5, 1921. Belt worn until February 3, 1921. *Change in symptoms and signs following application of belt:* Cough and expectoration for which belt was applied greatly relieved. *Condition improved.*

No. 3947. M. T. Male. Age thirty. Admitted November 18, 1920. Duration of disease two years. *Extent:* Far advanced pulmonary tuberculosis. Considerable involvement throughout both lungs. Cavity formation in upper right. Chronic laryngitis. Chronic interstitial nephritis. *Character of symptoms:* Severe cough and expectoration. Temperature up to 100° — 101°. Weakness, loss of weight. Loss of appetite. Belt applied January 5, 1921. Belt worn to date. *Change in symptoms and signs following application of belt:* Temperature and pulse down to normal. Considerable improvement in cough and expectoration. *Condition improved.*

No. 3950. J. C. Male. Age twenty-seven. Admitted November 22, 1920. Duration of disease about six months. *Extent:* Far advanced pulmonary tuberculosis. Marked involvement throughout right lung. Cavity formation in upper left. Tuberculous laryngitis. *Character of symptoms:* Severe cough and expectoration. Extreme weakness. Loss of weight, night sweats. Temperature 102°. Belt applied December 4, 1920. Belt worn until January 14, 1921. *Condition worse.*

No. 3955. E. B. Female. Age twenty-five. Admitted November 29, 1920. Duration of disease about four years. *Extent:* Advanced pulmonary tuberculosis. Marked involvement throughout both lungs. Annular shadows in both uppers. Diaphragmatic adhesion on the left. *Character of symptoms:* Temperature up to 100°. Severe cough and expectoration. Weakness, loss of weight. Belt applied January 23, 1921. Belt worn to date (belt loosened every night). *Change in symptoms and signs following application of belt:* Temperature down to normal (with rare exceptions up to 99.2°). Cough and expectoration improved. Slight gain in weight. *Condition improved.*

No. 3962. C. S. Female. Age twenty-six. Admitted December 8, 1920. Duration of disease about three years. *Extent:* Advanced pulmonary tuberculosis. Considerable involvement of both lungs. Annular shadow in upper right. Bronchial changes throughout both bases. *Character of symptoms:* Occasional fever up to 99.6°. Weakness. Pain in the shoulders. Mild digestive disorders. Considerable cough and expectoration. Belt applied February 15, 1921. Belt worn to date. *Change in symptoms and signs following application of belt:* Cough and expectoration improved. Temperature normal. *Condition slightly improved.*

No. 3970. A. S. Male. Age thirty-seven. Admitted December 25, 1920. Duration of disease about six months. *Extent:* Far advanced pulmonary tuberculosis. Considerable involvement throughout both lungs especially the left. Consolidation of whole upper and one-half of lower lobe on left. Cavity formation upper left. *Character of symptoms:* Severe cough. Extreme weakness. Very high temperature at times reaching 104°. Pneumothorax attempted on left side: unsuccessful on account of adhesions. Belt applied February 28, 1921. Belt worn to date. *Change in symptoms and signs following application of belt:* Temperature dropped down to normal on second day after belt was applied. Great improvement of all symptoms. *Condition greatly improved.*

No. 3977. C. G. Male. Age thirty-six. Admitted January 11, 1921. Duration of disease about two and a half years. *Extent:* Advanced pulmonary tuberculosis. Marked involvement of both lungs with fibrous changes and inflammatory mottling in both uppers. Fibrous changes in both hili especially in the right. Adhesions to right diaphragm. *Character of symptoms:* Severe cough and expectoration. Daily temperature up to 101°. Weakness, loss of appetite. Belt applied January 23, 1921. Belt worn until March 24, 1921. *Change in symptoms and signs following application of belt:* Temperature down to normal. Cough and expectoration greatly improved. Appetite improved, gaining weight. *Condition greatly improved.*

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THE SPLEEN AS AN APPROXIMATE INDEX OF TUBERCULOUS INVOLVEMENT AFTER SUBCUTANEOUS INFECTION

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In studying the effect of therapeutic procedures it is common practice to resort to the use of an easily infected animal. This is exemplified, for instance, in testing the value of an antipneumococcus serum, for which purpose the highly susceptible mouse is made use of. It is true that in tuberculosis the time interval of infection and development of disease is greatly increased over that necessary in experiments in the acute diseases, so that in this case it seems even more desirable to use animals with the greatest susceptibility to experimental inoculation. The chronicity of the course of tuberculosis in itself magnifies the possible pathological differences, besides introducing marked individual variations. As the time of study increases the possibility for uniformity of results naturally becomes less. It is for this reason that comparative studies on the resistant animals, for example, dogs, rabbits, rats and mice, possess decided disadvantages over such studies in the susceptible guinea pig. It is true that it might be argued that the course of the disease in the guinea pig is so rapid that slight differences might be overlooked. Here we are compelled to decide whether fine details in observation are not well worth sacrificing, to avoid the errors encountered by a too prolonged period of observation necessary when using the highly resistant animal. It might even be ventured that the lack of value of specific or chemotherapeutic studies on man in tuberculosis can be accounted for by the prolonged chronic and uncertain course of the disease in this case.

It is not the purpose of this paper to dwell upon the detailed mechanism of tuberculous infection in the guinea pig, nor to attempt an anatomic description of this animal, since this has been done so excellently and elaborately by Krause (1) who also cites the earlier work on this subject by Arloing in 1892 and Oehlecker in 1907. We wish merely to report in rather more empiric fashion the results of the inoculation of graded doses of virulent human tubercle bacilli into guinea pigs under approximately uniform conditions of experiment. Krause's experiments were performed in almost identical fashion to that used in the experiments to be reported below, except that he injected large doses of bacilli subcutaneously, although he at times utilized two different strains of bacilli, one of high and one of moderate virulence. Since it has been observed, in using graded doses of bacilli given subcutaneously to guinea pigs, that the spleen at definite intervals reveals certain approximate findings correlated to the general tuberculous condition of the animal, this organ will be given greater consideration in this paper.

Krause maps out the course of the bacilli from the subcutaneous site of inoculation as follows: To the superficial inguinal nodes, the deep inguinal nodes, the common iliac nodes, the plexus and nodes of the abdominal aorta, the thoracic duct, into the venous system and then into the lungs, tracheobronchial lymph nodes, spleen, liver and other organs. After the last (most central) node is passed, particles reach the thoracic duct and thence the venous system, from which all particles converge toward the lungs, through which they may pass or in which they may be arrested. Those particles that pass through the pulmonary blood vessels are distributed dispersively by the systemic arteries to the several organs and parts of the body. The spleen receives particles by way of the splenic artery alone. Such particles may pass through the spleen by way of the blood vessels or they may be fixed in the spleen. Those that pass through go direct to the liver by the splenic and portal veins. Those that are fixed may remain in the lumina of the smaller vessels or be carried out of these into the lymphatic system. In the lymphatic system they may be arrested in lymphoid collections (Malpighian bodies) or be carried further to the splenic node, the cisterna chyli, thoracic duct and venous system, whence they return to the lungs.

After large subcutaneous injections Krause found bacilli in all the nodes and tissues examined from four days after infection on. The bacilli had within this time passed all lymphatic barriers, had got from the lymph stream into the blood, had passed by the blood into the lungs, had left the lumina of the smaller blood vessels of the lungs, had gone into the pulmonary lymphatics and had by these been carried to the tributary tracheobronchial nodes.

Although the above data give valuable information it is unfortunate that for the sake of completeness studies of graded doses of bacilli were not included, since it is conceivable that small doses may act quite differently, especially as regards their rate of appearance in the various organs from very large doses.

Krause also well describes the evolution and spread of macroscopic changes from the point of inoculation in the guinea pig. The site of inoculation of bacilli exhibits acute subcutaneous reaction up to the ninth day after the infection. Beginning at six days, distinct changes are to be noted in the superficial inguinal nodes; at this time the latter are "slightly enlarged and a little more opaque than normal;" at twelve days "enlarged, opaque and with yellowish spots" (necrosis); at eighteen days, there is an abscess of the soft tissues and "proceeding cephalicwards a chain of five to seven enlarged nodes, of which the one next to the abscess is largest and shows necrotic spots." At six days the iliac node is "somewhat enlarged;" while at eighteen days it is "as large as a bean and necrotic." The first time that the spleen can be called grossly tuberculous is at twelve days, when it may show small, yellow tubercles; and at eighteen days and afterwards lesion is always well established. The paraortic nodes were noticeably enlarged from twelve days on. The lungs never exhibited gross tubercle,—up to twenty-six days. The first time that the tracheobronchial nodes were unquestionably grossly tuberculous was at twenty-two days, though before this there were suggestions of tubercle in these nodes.

Until considerable enlargement occurs, early gross tuberculosis of the tracheobronchials is difficult to determine. The nodes are often completely involved without a trace of necrosis. At eighteen days the retrosternal nodes were "enlarged, firm and opaque."

In summarizing, Krause states;

> By the method of tissue inoculation it has been shown that after subcutaneous (right groin) infection of guinea pigs with massive doses of tubercle bacilli, the bacilli are carried centralwards by the lymphatic stream and thence into the blood throughout the body with great facility and rapidity. At four days and earlier they have reached the iliac node of the inoculated side by way of the lymphatics. At four days and perhaps earlier they are present in the spleen. At four days they are also in the lung and tracheobronchial nodes. Most of those in the tracheobronchial nodes represent bacilli which have been carried out of the pulmonary blood vessels and thence over to

intrapulmonary lymphatics by which they drained to the nodes. . . . At any given time during the period of from four to nine days after infection there are more bacilli in the iliac node of the inoculated side than in the spleen or lungs or tracheobronchial nodes. . . . During this same period the bacillary contents of the spleen and tracheobronchial are so nearly equal that animal inoculation of these tissues produces approximately the same effects. . . . During the period from four to twenty-six days after infection there are more bacilli in the tracheobronchial nodes than in both lungs, which they drain. Gross changes appeared as follows: The first definite lesion in the superficial inguinal nodes at six days and the first necrosis at twelve days; the first suggestions of lesion in the right iliac node at six days, and the first undoubted lesion at twelve days; the first enlargement of the paraortic nodes at twelve days; the first undoubted changes in the spleen at twelve days; the first unquestionable lesion of the tracheobronchial nodes at twenty-two days; the first involvement of the retrosternal nodes at eighteen days; during the twenty-six days of the first part of the experiment the lungs never exhibited lesion.

The entire picture of guinea pig tuberculosis revealed to us by Krause, which has purposely been described in detail because of its value for elucidating this paper, depicts a certain fairly accurate but approximate quantitative involvement of this animal directly associated with the time element. So far as our own observations go, which have considered mainly the advanced macroscopic findings, they are entirely in accord with the findings recorded by Krause. They might even be considered as an addition to his data in which the time element has been extended and graded doses of the same organism studied. From the excellent data given us by Krause it is conceivable that the infection and development of disease in the guinea pig proceeds in a definite and methodical fashion in the majority of the cases and that there are certain localities or organs where this is especially to be noted, such as the lymph nodes and the spleen, in so far as his studies were carried. In a tabulation of nine animals in which the tuberculosis had progressed markedly, there is also noted this approximate correlation between the spleen findings and the general condition of the animal. The macroscopic tuberculous involvement of guinea pigs has for some time been used as an approximate index of the effect of various procedures upon the tuberculosis in these animals by Corper and his collaborators, especially when using graded doses of bacilli and the close relationship noted between the splenic involvement and the generalized tuberculosis, so that a general summing up of some of these findings seemed worthy of consideration.

All of the guinea pigs recorded in these data were infected by injecting the tubercle bacilli into the subcutaneous tissues of the left groin. Virulent human tubercle bacilli were used, and the amount of bacilli injected ranged usually from about 0.1 to 0.000,000,1 mgm. The animals were usually examined from four to seven weeks after infection. The results of the examination of guinea pigs thus studied are given in table 1, in which is recorded the involvement of the various lymph nodes (left inguinals, left iliac, tracheobronchials) and organs (liver, lungs and spleen), besides the total involvement of 151 guinea pigs infected with doses of virulent human tubercle bacilli, ranging from 0.1 to 0.000,000,1 mgm. and examined from four to seven weeks after infection.

The tabulated data resulting from the macroscopic examination and approximate grading of the tuberculous involvement of the organs of guinea pigs, given in table 1, reveals a definite relationship between the dose of bacilli used for infecting and the sequence of the disease involvement, correlating Krause's observations, in which the time element was found to be related to the macroscopic and microscopic involvement after the subcutaneous administration of large doses of bacilli. Besides this, there is noted a definite relationship between the splenic and total tuberculous involvement of the guinea pigs. The slight deviations recorded in this table might easily be accounted for by the fact that these data were obtained by more or less empiric recording methods and not by means of detailed studies as in the case of Krause's work.

Since table 1 does not bring out certain detailed points regarding the relation between the splenic and total tuberculous involvement in guinea pigs, the records of 279 guinea pigs are given in table 2 in which the graded tuberculosis of the spleen is correlated with the graded total macroscopic tuberculosis in these animals, regardless of the dosage of bacilli or the treatment administered during the course of the infection. In interpreting these results it must be remembered that a guinea pig may be given a total tuberculous rating of one plus while the spleen may be entirely negative, which is entirely consistent, when we consider that definite tuberculous changes may be found in the inguinal and iliac glands before the infection is macroscopically visible in the spleen. When, however, the spleen does show involvement the correlation seems to be fairly clear cut.

TABLE 1

The relation between the tuberculous involvement of the spleen and other organs of the guinea pig, following subcutaneous infection with different amounts of virulent human tubercle bacilli ※

AMOUNTS OF BACILLI USED FOR INFECTING IN MILLIGRAMS	NUMBER OF ANIMALS STUDIED	GRADE OF INVOLVEMENT*	ORGANS RECORDED						
			Left Inguinals	Left Iliac	Tracheo-Bronchials	Liver	Lungs	Spleen †	Total ‡
0.1	15	−	0	0	0	6	7	0	0
		+	0	0	1	6	7	0	0
		++	1	4	6	3	1	0	0
		+++	10	8	6	0	0	11	15
		++++	4	3	2	0	0	4	0
0.001	49	−	2	3	3	28	37	1	1
		+	1	9	10	12	10	4	3
		++	15	13	27	4	2	10	18
		+++	21	19	9	5	0	25	19
		++++	9	5	0	0	0	9	8
0.000,01	37	−	0	1	2	29	34	2	0
		+	3	4	10	5	3	1	6
		++	15	10	20	3	0	14	21
		+++	16	20	5	0	0	19	9
		++++	3	2	0	0	0	1	1
0.000,000,1	50	−	0	2	4	34	45	5	0
		+	9	13	13	10	4	1	15
		++	24	12	27	5	1	19	17
		+++	17	20	6	1	0	21	17
		++++	0	3	0	0	0	4	1

※ In table 1 no animals were recorded in which any factor such as treatment may have had an influence upon the infection.

* For the sake of uniformity in recording, the grade of involvement of the organs is classified from − to ++++, which is only intended to be approximate. This grading is taken merely to conform with the markings in use in the Research Department, in which the general tuberculous involvement of the guinea pig is thus recorded in previous publications.

† It is difficult to accurately grade the splenic tuberculous involvement, but for the sake of visual figurative approximation the gradings throughout this paper from − to ++++ indicate the following findings:

−, there is no tuberculosis macroscopically visible, nor is there any enlargement.

+, tubercles are visible but there is no enlargement of the spleen.

++, the spleen is enlarged 2 to 5 times and is tuberculous.

+++, the spleen is enlarged 5 to 10 times approximately and is tuberculous.

++++, the spleen is enlarged over 10 times approximately and is markedly tuberculous.

‡ The total or general tuberculous condition of the guinea pig is graded from − to ++++ in conformity with the records in previous communications from this laboratory.

−, no visible macroscopic tuberculosis.

+, distinctly enlarged local (left inguinal) and slightly enlarged iliac nodes.

++, enlarged inguinal and iliac nodes and slight involvement of the spleen.

+++, enlarged inguinal and iliac nodes, spleen markedly involved, tracheobronchial nodes enlarged and the lungs slightly involved.

++++, massive involvement of all important nodes in path of infection, spleen, lungs and liver.

A study and grading of the spleen and total involvement of 279 tuberculous guinea pigs given in table 2 reveals that there is a fairly exact correlation between the splenic involvement and the total involvement of this animal with tuberculosis which is evident with the earliest involvement of the spleen and thereafter.

TABLE 2

The spleen as an approximate index of the general tuberculous involvement of the guinea pig after infection with human bacilli ※

GRADE OF INVOLVEMEMT OF THE SPLEEN*	NUMBER OF ANIMALS	GRADE OF GENERAL INVOLVEMENT †				
		–	+	++	+++	++++
–	57	6	51	0	0	0
+	26	0	24	2	0	0
++	71	0	15	53	3	0
+++	102	0	1	35	63	3
++++	23	0	0	0	13	10

※ In table 2 are included the findings in pigs, both treated and untreated, since it has been noted that certain treatment may influence the general tuberculosis but this does not alter the relation between the total and tuberculous splenic involvement.

* The grade of splenic involvement is indicated by – to ++++ as follows:

–, no macroscopic tuberculosis or enlargement.

+, macroscopic tubercles but no enlargement.

++, spleen enlarged 2 to 5 times and tuberculous.

+++, spleen enlarged 5 to 10 times and tuberculous.

++++, spleen enlarged over 10 times and markedly tuberculous. (See note †, table 1.)

† The grade of general tuberculous involvement from – to ++++ conforms with the total involvement recorded under note ‡, table 1.

SUMMARY AND CONCLUSIONS

The macroscopic tuberculous involvement of guinea pigs, infected subcutaneously in the groin with human bacilli, follows a definite organ sequence which is related to the time interval as was pointed out by Krause, and can be correlated fairly well with the dose of bacilli used for infecting.

In the course of the infection and when the spleen begins to show tuberculous changes, this organ can be used as a fairly approximate gauge of the general or total tuberculous involvement of the guinea pig, especially when studies are being made in which are included a reasonably large series of animals.

We wish to acknowledge the kind aid in obtaining the data for this paper and valuable suggestions during its preparation contributed by Dr. H. J. Corper.

REFERENCE

(1) Krause, A. K.: Amer. Rev. Tuberc., 1920, iv, 135.

STUDIES ON THE INFLUENCE OF CARBON DIOXIDE ON RESISTANCE TO TUBERCULOSIS

THE EFFECT OF CARBON DIOXIDE ON THE TUBERCLE BACILLUS

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The resistance to tuberculosis which is evident at almost every postmortem performed on man has been variously explained as the result of a humoral antibody action, in the Ehrlich sense of the term, the entire gamut of antibodies having at some time or other come into consideration, or a specific cellular reaction or response in the phagocytic sense, as used by Metchnikoff; the lymphocyte, the polymorphonuclear leucocyte, the connective tissue cell, the endothelial cell, and other less prominent cells at times occupying the foreground. That some of these factors no doubt play a significant part cannot be denied; but analysis of any individual factor leaves much to be desired in the way of explanation. The excellent recent researches of Foot (1), Permar (2), and Karsner and Swanbeck (3) on the vascular endothelial cell leave very little doubt but that this cell plays a definite part in the cellular combat against the tubercle bacillus; the exact proportionate relation of this cell in resistance to tuberculosis, however, still remains to be disclosed. That the allergic reaction is in some way associated with resistance to tuberculosis, as was indicated in Koch's pioneer observations (4), seems to be borne out by the researches of Trudeau (5), Krause (6), Soper (7), Römer and Joseph (8) and others.

That there might be a purely chemical factor active in the determination of the individual resistance to tuberculosis seems to have been lost sight of, primarily because of the lack of any experimental evidence indicating this possibility. Upon entirely empiric clinical reasoning Weber (9) believed that he saw a relation between carbon dioxide and resistance to tuberculosis. He reasoned that the tubercle bacillus invades the body of almost all of mankind, yet only about ten per cent of all deaths are due to this disease; individuals who eat insufficiently are disposed to tuberculosis (Brehmer) and treatment benefits only in so far as it stimulates the appetite; carcinoma affects the strong, tuberculosis the weak; diabetics are highly susceptible to tuberculosis because there is a diminished carbon dioxide production as a result of the lack of power to combust or utilize sugar; that phthisis becomes arrested or ameliorated during pregnancy, in spite of the fact that the reverse might be expected, is explicable on the basis of the increased carbon dioxide contributed to the mother by the fetus, a condition which is changed after delivery, when tuberculosis again develops with renewed vigor; in cardiac conditions leading to venous stasis and accumulation of carbon dioxide there is a high so called "immunity" to tuberculosis, while children with pulmonary stenosis die early of this disease; the accumulation of carbon dioxide in the lungs in emphysema is the source of the high relative immunity of these cases to tuberculosis; hunchbacks with their contracted thoraces are spared from tuberculosis, because the lungs have not developed in relative proportion to the other organs and are called upon to dispose of a greater amount of carbon dioxide; primary tuberculosis of muscle is rare because of its high content of carbon dioxide; while the apex of the lung is more readily involved by tuberculosis because it has less carbon dioxide than the other parts; and finally the rest treatment of tuberculosis is beneficial because the horizontal position causes a retention of more venous blood rich in carbon dioxide at the apex of the lung than in the erect posture, thus imitating the Bier stasis treatment.

Weber began treating pulmonary tuberclosis in 1889 by giving sodium bicarbonate followed by hydrochloric acid by mouth, one-half hour before meals, in order to generate carbon dioxide in the stomach as a means of increasing the carbon dioxide content of the blood and tissues. Later, in 1901, realizing the impossibility of administering sufficient sodium bicarbonate and hydrochloric acid to produce an appreciable increase in carbon dioxide in the body, he sought other means to accomplish this end. Reasoning that a man of 150 pounds exhales about 500 litres of carbon dioxide daily and by comparison a fetus of about 3 pounds should produce about 10 litres, the addition of the latter amount, therefore, should be necessary to arrest the disease, if conclusions can be drawn from the arrest of tuberculosis in pregnancy. The production of this amount would require at least 40 grams of sodium bicarbonate and could not be given by stomach feasibly; therefore, a substance combustible to carbon dioxide in the body would be a desirable adjuvant. For this purpose he used levulose feedings of 50 to 100 grams daily over a period of months and also gave subcutaneous injections of olive oil and vaseline or paraffine oil in the belief that the latter produced carbon dioxide in the body. As a matter of fact, paraffine oil canot give rise to carbon dioxide through the metabolic activity of the body.

In 1902 he finally outlined his complete treatment. To the less severe cases of tuberculosis he gave sodium bicarbonate and hydrochloric acid by mouth, with feedings of levulose to reinforce the carbon dioxide production, and to the more severe cases he combined the foregoing with subcutaneous injections of liquid paraffine in 10 gram amounts twice daily, reaching in some cases as high as 200 injections.

That carbon dioxide may have an influence upon the growth of the tubercle bacillus was indicated by the studies of Wherry and Ervin in 1918 (10). In studying the effect of gaseous environments upon the growth of bacteria, they found that complete removal of carbon dioxide prevented the growth of tubercle bacilli even in the presence of all the other gaseous constituents of the air. The bacilli remained in a non-reproductive state but viable, as shown by guinea pig inoculation two weeks later. They found also that, when oxygen and carbon dioxide reach an optimal point, growth starts. Under atmospheric carbon dioxide (7 mm.) pressure, there was growth; but at higher pressures (77 mm.) there was no growth of the tubercle bacillus. They called attention to the fact that in a closed system not only does carbon dioxide accumulate but the oxygen supply diminishes. Their experiments, although significant in indicating that carbon dioxide would inhibit the growth of tubercle bacilli, were not elaborate enough to give any idea as to the approximate concentrations or conditions under which this occurred.

Experiments recently performed with the gonococcus by Rockwell and McKann (11) indicate that bacteria manifest evidences of respiration before evidences of their growth appear and that growth is not visible until considerable changes in the gaseous environment (in sealed tubes) have occurred. The gaseous constituents changed from carbon dioxide 0.5 per cent, and oxygen 19 per cent, to carbon dioxide 6 per cent, and oxygen 2.5 per cent. In pure hydrogen 3 per cent carbon dioxide concentration was attained. Moisture plays some rôle, but is of far less importance than the gases.

The carbon dioxide tension of the tissues may be approximated from the studies made by Haggard and Henderson (12), who investigated the gas tensions of the abdominal cavity, alveolar air and blood. They state that the carbon dioxide tension of the abdominal air (normally approximating a tension of 35 to 42 mm. mercury) soon becomes equivalent to that of the pulmonary alveolar air and of the arterial blood, and that under abnormal conditions (experimental acidosis) the carbon dioxide tension in the abdominal air falls in close correspondence to the arterial carbon dioxide tension (as low as 16 to 23 mm. mercury). In man gaseous studies have been made in cases of tuberculosis with pneumothorax, to gain information on the proper gas mixture to be used in artificial pneumothorax treatment. Fortunately the data have been often obtained and well worked up, so that their accuracy is undoubted. Webb, Gilbert, James and Havens (13), in a study of a large number of cases, found that after a short interval of time, regardless of whether nitrogen, oxygen or atmospheric air was injected into the pleural cavity, the composition of the gas rapidly approached that of alveolar air. The carbon dioxide content of the pleural gases varied from about 5 to about 10 per cent. Tobiesen (14) found that an exudative pleuritis caused an increased carbon dioxide (to about 10 per cent) content of the pleural gases as compared to a nonexudative type (about 6 per cent). The carbon dioxide content of the pleural gases increases postmortem in man. Tachau and Thilenius (15), using more exact methods of gas analysis, corroborated the above findings. In pneumothorax cases without an exudate, the carbon dioxide content of the pleural gases ranged from about 6.5 per cent to 8.5 per cent and the oxygen content varied from 1.9 to 6.2 per cent, while cases with an exudate contained from 10.5 to 12.7 per cent carbon dioxide and an oxygen content of less than 1 per cent.

It is known that certain chemical substances easily enter the cells and tissues, while others are found only in the surrounding fluids of the body. The high potassium content of the cell, as compared to the high sodium content of the fluids of the body, is a classical example of this. Fortunately the recent observations of Jacobs (16) help to elucidate the mechanism of this action. He found that carbon dioxide is incomparably more toxic for toad tadpoles than are solutions of hydrochloric, oxalic, salicylic, formic, acetic or butyric acids of the same hydrogen ion concentration and, in the presence of sufficient bicarbonate to give practically a neutral reaction to the solution, the toxic properties of CO_2 for tadpoles are unchanged. Jacobs interpreted these results as being due to the fact that the H_2CO_3, whose dissociation is held in check by the bicarbonate, can freely enter cells (perhaps as CO_2), while the bicarbonate cannot; the carbonic acid dissociating when within the cells to the extent permitted by the new conditions of equilibrium prevailing there, which may easily result in a hydrogen ion concentration higher than that of the surrounding medium. This conception is fortified by his observations with the flowers of *Symphytum peregrinum*. These contain a natural indicator sensitive to carbonic acid. An "artificial cell" was prepared by him for illustration. With it he produced a condition of intracellular acidity with a slightly alkaline solution of CO_2 in M/2 $NaHCO_3$, almost as effectively as with a solution of CO_2 in distilled water, though the hydrogen ion concentration of the latter solution is approximately four thousand times as great as that of the former. He believed that the ability of neutral and slightly alkaline solutions containing CO_2 to produce intracellular acidity is probably due to at least two factors, namely, the weakness of H_2CO_3 as an acid and the lipoid solubility of CO_2 or H_2CO_3 or both, and the lack of such solubility in the case of bicarbonates.

The investigations of the effect of carbon dioxide upon the tubercle bacillus reported in this communication were begun as a part of a study of the effect of various gases and pressures upon the growth of the tubercle bacillus. The results with carbon dioxide proved so interesting and valuable, however, that the studies were elaborated and applied to animals. Our greatest difficulty was to develop a method suitable for the determination of carbon dioxide in small amounts of gas—not too delicate to be impracticable and still of sufficient accuracy to be well adapted for the determinations at hand. The usual methods of analysis for carbon dioxide require comparatively large volumes of the gas and rather bulky and burdensome apparatus. The Hempel apparatus used by Tachau and Thilenius requires about 20 or more cc. and the Haldane apparatus, used by Webb and his colleagues, about 30 or more cc. for each analysis. These methods accomplish the analysis of carbon dioxide by removing it by absorption, measuring the decrease in volume of the original gas and then calculating the percentage volume or partial pressure of the carbon dioxide. Direct gravimetric methods have not been placed on an easily working basis presumably for two reasons: first, the great possibility of error from air contamination and consequent alteration, which requires that the analyses be performed in a closed system; and second, the difficulty of measuring small amounts of carbon dioxide by any gravimetric system. Tashiro (17) has perfected the biometer, by means of which he is able to measure carbon dioxide in almost incredibly small amounts. The principle of his method is to note with a lens the precipitation of barium carbonate on the surface of a drop of barium hydroxide, in a suitably closed vessel (the biometer), which is filled with a carbon dioxide-free gas.

It was soon recognized that the needs in the work to be reported lay between the above two extremes. It was necessary to analyse gases containing from 1 to 10 per cent carbon dioxide in an available few cubic centimetres of gas mixture sample.

In preliminary experiments it soon became evident that the barium carbonate precipitate from a barium hydroxide solution possessed possibilities for a system of analysis, provided these small amounts could be utilized for a quantitative method. An attempt to determine nephelometrically the turbidity occasioned by the precipitated carbonate revealed a multiplicity of difficulties, some of which could not be overcome. The greatest difficulty was met when two suspensions of equal amounts of carbonate were prepared and were found to reflect light at different rates and thus give entirely different quantitative values for the same amount of CO_2 It was, therefore, finally decided to measure the precipitated barium carbonate volumetrically.

METHOD

In order to prepare suitable standards of known carbon dioxide content in both gaseous and liquid form it was essential to use reagents of definite strength, capable of delivering known volumes of carbon dioxide in gaseous form or containing a known amount of carbon dioxide in water soluble carbonate form. For this purpose a solution of sodium carbonate (or bicarbonate) was used and the calculations were made as follows:

Molecular weight of $Na_2\,CO_3$ = 106

Molecular weight of CO_2 = 44

$106 : 44 :: 1 : x$

$x = 0.41509$ gram CO_2, obtained from 1 gram anhydrous $Na_2\,CO_3$ at 0°, 760 mm. B.P.

The weight of 1 cc. of carbon dioxide at 0° 760 mm. B.P. as given by Fresenius (18) is 0.001965 gram, therefore:

$$\frac{0.41509}{0.001965} = 211.241 \text{ cc. } CO_2\text{, obtained from 1 gram anhydrous } Na_2\,CO_3 \text{ at } 0° \text{ 760 mm. B. P.}$$

The amount of sodium carbonate required to produce 1 cubic centimetre of carbon dioxide is

$$\frac{1}{211.241} = 0.00473 \text{ grams } Na_2\,CO_3\text{, necessary to produce 1 cc. } CO_2 \text{ at } 0° \text{ 760 mm. B.P.}$$

These figures have to be corrected to values for the temperature, barometric pressure and vapor tension in which the experiments are being performed. The average barometer pressure of our laboratory is 630 mm. and the average temperature is 20°C. Dennis (19) gives the following formula for the correction of volumes of gases:

$$v_0 = v_1 \frac{p_1 - m}{760\ (1 + 0.00367\ t_1)}$$

in which v_1 is the observed volume, p_1 the observed pressure, t_1 the observed temperature and m the tension of aqueous vapor. Our problem, however, is to compute v_1 at the desired t_1 and p_1 from the known v_0, t_0 and 760; so adapting the formula, it becomes

$$v_1 = v_0 \frac{760\ (1 + 0.00367\ t_1)}{p_1 - m}$$

When the volume of a gas changes it is evident that the weight of the gas is inversely proportional to the volume change. That is, if 1 cc. (V_1) becomes 2 cc. (V_2) and t and m remain constant, then 1 cc. of V_2 weighs only one-half of one cc. of V_1 which may be expressed as follows:

$$V_0 : V_1 :: W_1 : W_0, \text{ or}$$

$$W_1 = \frac{W_0 V_0}{V_1}$$

The volume of V_1 has just been adapted from Dennis; therefore, to obtain the weight of V_1 we combine the two formulae and obtain

$$W_1 = \frac{W_0 V_0}{V_0\ 760 \dfrac{(1 + 0.00367\ t_1)}{p_1 - m}}$$

from which we may compute the weight of 1 cc. of gas for any desired pressure and temperature if we know the weight at 0°, 760 mm. B.P. To compute the weight of 1 cc. of CO_2 at 630 mm. and 20°C. we substitute the known values for W_0, which is 1.96507 mgm. $V_0 = 1$, $t = 20$, $p = 630$, $m = 17.396$ and obtain:

$$W_1 = \frac{1.96507 \times 1}{1 \times 760 \times \dfrac{1 + (0.00367 \times 20)}{630 - 17.396}}$$

$W_1 = 1.4973$ mgm. = weight of 1 cc. CO_2 at 20°, 630 mm. B.P.

To determine the number of cc. of CO_2 at 20°, 630 mm. B.P., available from 1 gram $Na_2\ CO_3$:

0.0014973 gram = weight of 1 cc. CO_2 at 20°, 630 mm.

0.41509 gram CO_2 is obtained from 1 gram $Na_2\ CO_3$ at 0° 760 mm.

Therefore,

$\frac{0.41509}{0.0014973}$ = 277.225 cc. CO_2 is obtained from 1 gram $Na_2\ CO_3$ at 20° 630 mm. B.P.

To determine the amount by weight of anhydrous $Na_2\ CO_3$ required to produce 1 cc. CO_2 at 20°, 630 mm., we consider that 1 gram $Na_2\ CO_3$ at 20°, 630 mm., forms 277.225 cc. CO_2; therefore,

$\frac{1}{277.225}$ = 0.003607 gram $Na_2\ CO_3$, is necessary to produce 1 cc. CO_2 at 20°, 630 mm. B.P.

This last figure 0.003607 gram Na_2CO_3, or 3.61 mgm., is the solution equivalent of 1 cc. of CO_2. A stock standard solution is then prepared by dissolving 361 mgm. of anhydrous sodium carbonate, c.p., in 100 cc. distilled water. If 1 cc. of the stock solution is then diluted to 100 cc., 1 cc. is equivalent in carbon dioxide to 1 cc. of a 1 per cent CO_2 air mixture. If 2 cc. of the stock solution are used, then 1 cc. becomes equivalent to 1 cc. of a 2 per cent CO_2 gas mixture, etc.

It was observed that the precipitate of barium carbonate produced by the equivalent of 1 cc. of a 1 per cent CO_2 gas mixture could be collected and measured with reasonable accuracy in a Hopkins centrifuge tube (20) and occupied 0.002 cm. The technique used is as follows: Clean the Hopkins centrifuge tube thoroughly, add 1 cc. of the desired solution with a volumetric pipette, add 5 cc. of clear saturated barium hydroxide solution, kept under pure paraffine oil to avoid air and CO_2 contact. Quickly superimpose 1 cc. of CO_2 free paraffine oil and centrifugate five minutes at about 2000 r.p.m. It is frequently necessary to stir the sediment gently with a fine wire and centrifugate a second time to insure a uniform and even packing of the precipitate. In this way it was found that 1 cc. solution, equivalent to 1 cc; of a 1 per cent CO_2 gas mixture, gave a precipitate of barium carbonate occupying 0.002 cc.; and 1 cc. solution, equivalent to 1 cc. of a 2 per cent CO_2 gas mixture, a precipitate occupying 0.004 cc., etc., as recorded in table 1 (see figure 1).

Having determined the volume occupied by the precipitate of barium carbonate obtained from the solution equivalent of the sodium carbonate, volumetric gas mixtures of carbon dioxide were prepared and 1 cc. of the gas mixture was placed in a closed system, to which was added 5 cc. of clear barium hydroxide, avoiding air contact. After being thoroughly mixed in the closed system, the barium hydroxide solution and its contained precipitate of carbonate were carefully run into a Hopkins centrifuge tube, quickly superimposed with 1 cc. paraffine oil and centrifugated. The pure carbon dioxide was generated by adding a dilute mineral acid to a concentrated solution of sodium carbonate. This pure CO_2 was permitted to enter a completely water filled graduated reservoir, from which it could be obtained in definite amounts as needed. A known CO_2 gas mixture was then prepared as follows: The graduated vessel containing the pure CO_2 was connected with glass tubing to a one litre volumetric flask, the glass tubing extending to the bottom of the flask. Ten cc. of mercury were permitted to run into the pure CO_2 chamber. The mercury displaced 10 cc. of CO_2 and forced it over to the bottom of the mixing flask. The CO_2, being a heavy gas, remained for a short interval at the bottom of the flask, permitting the displacement of an equal volume of air at the top. The flask was closed the instant the CO_2 completely entered. In this way a fairly accurate one per cent CO_2 gas mixture in air was prepared. Similarly, a 2 per cent, 3 per cent, etc., mixture may be prepared.

The next step in the analysis consisted in mixing the measured gas, containing carbon dioxide, with barium hydroxide to precipitate the carbonate. For this purpose the Van Slyke apparatus (21) for studying the alkali reserve of the blood was found most suitable. This apparatus combines several advantages. It is a mercury pump suitable for drawing the gas into a closed system without loss; it is suitably calibrated; it permits the subsequent addition of solutions without loss of any of the contained gas; and the mixing of the gas and aqueous barium hydroxide solution by simply raising and lowering the mercury leveling bulb. In order to transfer the gas mixture to the Van Slyke apparatus, use was made of the plan given in the diagram shown in figure 2. This depicts capillary glass and rubber tubing completely filled with mercury, to avoid loss of carbon dioxide or change in composition of the gas to be analyzed. The details here are omitted because of the obvious simplicity of the apparatus.

TABLE 1

Volumetric determinations of the precipitate of barium carbonate corresponding to gas volumes obtained from the solution equivalent of carbon dioxide

STOCK Na_2CO_3 SOLUTION: (3.61 MGM. PER CC.)	DILUTED TO	EQUIVALENT TO GAS MIXTURE	VOLUME OF Ba_2CO_3 PRECIPITATE
cc.	*cc.*		*cc.*
1	100	1 cc. 1% CO_2	0.002
2	100	1 cc. 2% CO_2	0.004
3	100	1 cc. 3% CO_2	0.006
4	100	1 cc. 4% CO_2	0.008
5	100	1 cc. 5% CO_2	0.010
6	100	1 cc. 6% CO_2	0.012
7	100	1 cc. 7% CO_2	0.014
8	100	1 cc. 8% CO_2	0.016
9	100	1 cc. 9% CO_2	0.018
10	100	1 cc. 10% CO_2	0.020

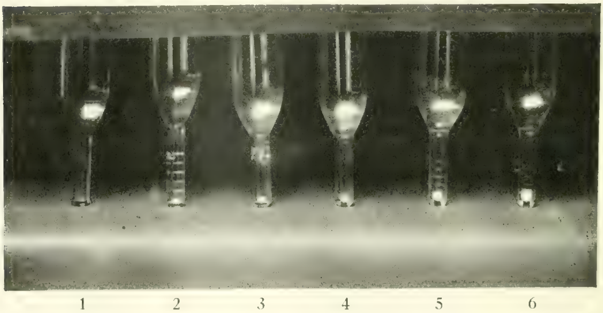

FIG. 1. SHOWING HOPKINS TUBES WITH CENTRIFUGATED SEDIMENTS OF BARIUM CARBONATE, PREPARED FROM THE SOLUTION EQUIVALENTS OF SODIUM CARBONATE

Reading from left to right tube 1 contains only the hydroxide, without carbonate and precipitate. The readings of tubes 2 to 6 are as follows:

	Contains solution Na_2CO_3 equivalent to	*Volume of Ba_2CO_3 precipitate*
Tube 2	1 cc. 1 per cent CO_2	0.002
Tube 3	1 cc. 2 per cent CO_2	0.004
Tube 4	1 cc. 3 per cent CO_2	0.006
Tube 5	1 cc. 4 per cent CO_2	0.008
Tube 6	1 cc. 5 per cent CO_2	0.010

An analysis is performed as follows: The pressure tubing connecting the Van Slyke apparatus and the container of the gas mixture is clamped close to the gas reservoir. A certain amount of room air is present in the tubing attached to capillary tube, *a*. This air is first removed by drawing it into the main chamber of the Van Slyke apparatus by lowering the leveling bulb, then expelling the gas through cup *b*. This is repeated until a metallic click is heard when the mercury is permitted to return, indicating a total absence of air.

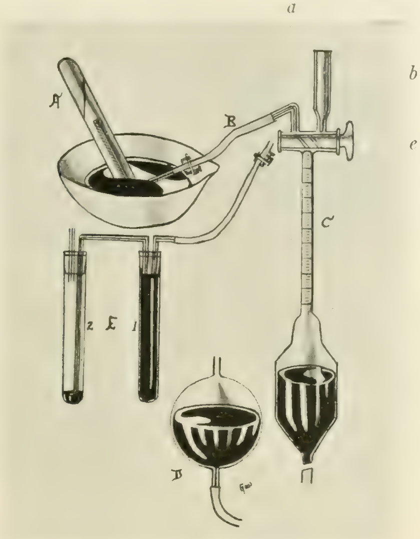

FIG. 2. DIAGRAMMATIC DRAWING OF APPARATUS USED FOR COLLECTING, STORING AND ANALYZING GAS FROM CULTURE TUBES

A. A culture tube, originally sealed, but now broken under mercury. It is held in place by a clamp. B. Capillary tube, filled with mercury, inserted into the open end of the culture tube and connected with the capillary tube of the Van Slyke apparatus. C. Van Slyke apparatus. D. Mercury leveling bulb. E. Gas reservoir. Tube 1 and pressure tubing leading from it are completely filled with mercury, and the tubing is clamped at its distal end. When the reservoir is attached to the Van Slyke apparatus, the clamp is opened, the gas is forced over by raising the leveling bulb and the displaced mercury is forced into tube 2.

The screw clamp on the pressure tubing is then removed and exactly 1 cc. of gas is drawn into the apparatus, as determined when the mercury in the apparatus and in the leveling bulb are level. Six cubic centimetres of clear barium hydroxide are placed in cup *b*, and about 5 cc. of this are run into the main mixing chamber in such a way that the gas in it is completely retained. This is accomplished by connecting stop cock *e* with cup *b* and gradually lowering the leveling bulb until about 1 cc. remains in *b*, when stop cock *e* is turned off. The mercury leveling bulb is placed in a position slightly lower than the mercury level in the mixing chamber, while the next step is being performed. The barium hydroxide remaining in cup *b* is quickly removed, and the cup is twice washed with distilled water; then 1 cc. of CO_2 free distilled water is placed in it. The gas and barium hydroxide are then mixed by raising and lowering the mercury leveling bulb gently. The pressure tubing is removed from capillary tube *a*, and the barium hydroxide and carbonate expelled through this into a Hopkins centrifuge tube. A small amount, of course, remains in the capillary tube. To wash this out, draw into the main chamber the water placed in cup *b*, subsequently adding it to the contents of the Hopkins centrifuge tube; then quickly superimpose 1 cc. of paraffine oil and centrifugate at a uniform rate of speed. In this way known CO_2 gas mixtures were prepared and analyzed; and the resulting precipitates measured volumetrically with the results given in table 2. (See figures 3 to 8.)

TABLE 2

Volumetric examination of the precipitate of barium carbonate obtained from carbon dioxide in certain percentage air mixtures

PURE CO_2 DILUTED TO 1 LITRE WITH AIR	CO_2 AIR MIXTURE IN PERCENTAGE	AMOUNT OF GAS USED FOR EXAMINATIONS	VOLUME OF Ba_2CO_3 PRECIPITATE
cc.	*per cent*	*cc.*	*cc.*
0	Atmosphere	1	0
10	1	1	0.002
20	2	1	0.004
30	3	1	0.006
40	4	1	0.008
50	5	1	0.010
60	6	1	0.012
70	7	1	0.014
80	8	1	0.016
90	9	1	0.018
100	10	1	0.020

Each gas mixture was tested at least five times and the results were found to be entirely uniform. The analytical studies for carbon dioxide consisted mainly in determining the carbon dioxide content of the gases in culture tubes. The tubes studied were either merely cotton paraffine stoppered, rubber stoppered or glass sealed. To obtain the gas from the cotton and rubber stoppered tubes a hypodermic needle was attached to pressure tubing, the tubing was clamped just as close to the needle as possible, the needle was inserted through the stopper and the tubing attached to capillary tube *a* of the Van Slyke apparatus. As a rule the air in the tubing is removed as previously described; then the clamp is opened and the gas drawn into the main chamber. It may then be transferred to a mercury filled reservoir to be utilized as needed. The glass sealed tubes required a slightly different technique to obtain the gas. One end of the tube was scratched with a file and broken under mercury in a suitable dish. The other end was kept in a vertical position by a clamp. A mercury filled capillary tube which had been attached to the Van Slyke apparatus was inserted under the open end and the gas withdrawn into the gas free Van Slyke apparatus (see figure 2).

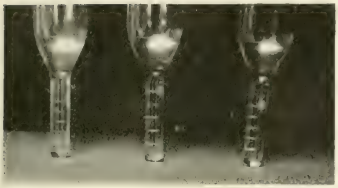

FIG. 3

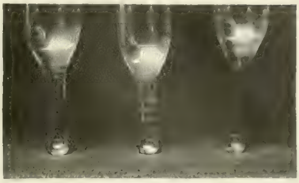

FIG. 4

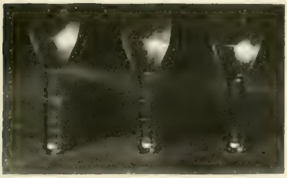

FIG. 5

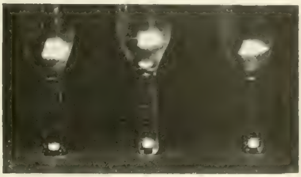

FIG. 6

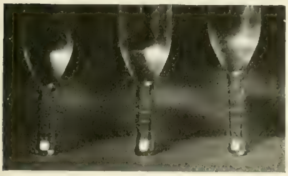

FIG. 7

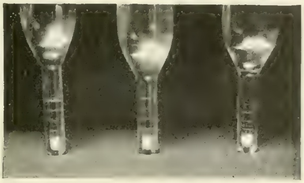

FIG. 8

FIG. 3. NO APPRECIABLE PRECIPITATE IN HOPKINS TUBES AFTER 3 ANALYSES OF 1 CC. EACH OF ATMOSPHERIC AIR

FIG. 4. CENTRIFUGATED SEDIMENTS OF BARIUM CARBONATE IN HOPKINS TUBES

Three analyses of 1 cc. each of a 1 per cent CO_2 gas mixture. The precipitate occupies 0.002 cc. each.

FIG. 5. CENTRIFUGATED SEDIMENTS OF BARIUM CARBONATE IN HOPKINS TUBES

Three analyses of 1 cc. each of a 2 per cent CO_2 gas mixture. The precipitate occupies 0.004 cc.

FIG. 6. CENTRIFUGATED SEDIMENTS OF BARIUM CARBONATE IN HOPKINS TUBES

Three analyses of 1 cc. each of a 3 per cent CO_2 gas mixture. The precipitate occupies 0.006 cc.

FIG. 7. CENTRIFUGATED SEDIMENTS OF BARIUM CARBONATE IN HOPKINS TUBES

Three analyses of 1 cc. each of a 4 per cent CO_2 gas mixture. The precipitate occupies 0.008 cc.

FIG. 8. CENTRIFUGATED SEDIMENTS OF BARIUM CARBONATE IN HOPKINS TUBES

Three analyses of 1 cc. each of a 5 per cent CO_2 gas mixture. The precipitate occupies 0.01 cc.

THE EFFECT OF CARBON DIOXIDE UPON THE GROWTH AND VIABILITY OF TUBERCLE BACILLI IN CULTURE TUBES

For determining the effect of carbon dioxide upon the growth of the tubercle bacillus a special culture tube was devised (see figure 9), in which a reasonably accurate concentration of carbon dioxide could be generated, as was revealed by numerous preliminary tests and analyses. The essential parts of this culture tube was a 6 × 1 inch heavy-walled

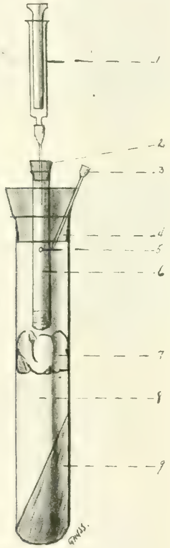

Fig. 9. Diagrammatic Drawing of Apparatus Used for Growing Bacteria in Known Volumes of Carbon Dioxide

1. Syringe for placing reagent in generating chamber. *2.* Rubber stopper. *3.* Needle for escape of displaced air. *4.* Rubber stopper. *5.* Small opening in generating tube for diffusion of gases. *6.* Small test tube in generating chamber. *7.* Sterile cotton plug. *8.* Air space of large test tube. The space occupied by the cotton plug plus the air space in the generating chamber totals approximately 50 cc. *9.* Ten cc. of culture medium.

bacteriological test tube, in which was a uniform slant (10 cc.) of culture medium, with a sterile cotton plug protecting it against contamination. In the mouth of this tube was a one-hole rubber stopper (no. 5), into which was inserted the generator tube, which was a small 4 × 1/2 inch heavy walled bacteriological test tube, rubber stoppered and with a small hole about 1 mm. in size blown into the side just below the point of insertion into the large one-hole rubber stopper. The purpose of the hole was to allow easy transfer of the gas from the small generator tube into the large reservoir of the culture tube. With a known air space in the large tube above the culture medium enough sodium carbonate could be placed in the generator tube, to which was added an excess of a mineral (dilute sulphuric) acid to generate any amount of carbon dioxide, after the medium had been seeded with tubercle bacilli, to give the desired concentration of this gas in air.

The procedure was carried out as follows: After planting tubercle bacilli on the glycerine agar the sterile cotton plug was inserted to a level below that reached by the generator tube. Into the generator tube was placed an amount of sodium carbonate sufficient to give the desired concentration of carbon dioxide in the volume of gas of the culture tube. The one-hole rubber stopper, containing the generator tube stoppered with a solid rubber stopper, was then carefully inserted into the large culture tube, care being taken to have no leakage around the rubber stoppers. An excess of dilute sulphuric acid was then drawn into a syringe and injected through the rubber stopper of the generator tube into the sodium carbonate. To allow an escape of the contained excess of air, a small hypodermic needle was inserted through the large one-hole rubber stopper into the culture tube and was retained there until air equilibrium had been established and the generation of carbon dioxide had ceased. The carbon dioxide being a heavy gas remained in the generator tube, or dropped to the bottom of the large culture tube for a sufficient period to prevent any loss of this gas: it would then slowly diffuse throughout the culture chamber after the gas escape needle had been withdrawn. After removal of both needles the gases were held in a practically sealed chamber. In the series in which a complete absence of carbon dioxide was desired, 1 cc. of a strong sodium hydroxide solution was placed in the generator chamber to absorb the carbon dioxide as it was formed.

In the series in which atmospheric air was used the tubes were merely stoppered with cotton plugs which had been slightly paraffined and were further covered with paraffine cloth after inoculation. In the series in which pure carbon dioxide was used a continuous stream of pure carbon dioxide, prepared from chemically pure sodium carbonate and dilute sulphuric acid, was passed through the rubber stoppered culture tubes, the gas entering by one hypodermic needle and the air passing out of the other until it was reasonably assured that all of the air had been displaced by carbon dioxide, when both hypodermic needles were withdrawn. In this entire cultural study a few factors had to be left to take care of themselves, such as the solubility of carbon dioxide in the culture medium, a slight escape of carbon dioxide through the needle used for adjusting the gas to atmospheric pressure and a slow solubility of carbon dioxide in rubber to which Haldane (22) has called attention and which was of some consequence in some of the other experiments to be given in this paper. These factors, however, proved of no importance in this part of the study except in the cases where the carbon dioxide content was over 15 per cent. Here perceptible loss was noted, especially as revealed by the gas analyses at the end of the experiment. Since, however, the significant findings occurred in concentrations below 15 per cent, these findings proved negligible.

In each gas series, four different strains of tubercle bacilli were studied, an old laboratory culture of a virulent human, a freshly isolated highly virulent human (Blum), an old laboratory culture of avirulent bovine (Bovine D), and a recently isolated culture of virulent bovine bacilli; and of each strain three tubes of 5 per cent glycerine agar were inoculated, except in the case of the virulent human strain (Blum), of which six tubes were inoculated, on account of its poorer growth upon artificial media (glycerine agar). Observations of the growth were made at weekly intervals for one month at 37.5°C., after which the gas contained in two-thirds of the tubes was analyzed for carbon dioxide and the stoppers removed to allow easy access of atmospheric air, and observations continued for another month at incubator temperature to note whether carbon dioxide had merely had an inhibitory action upon the cultures or had actually been tuberculocidal. The results of these cultural studies and analyses are given in table 3.

An examination of table 3 reveals that the four strains of human and bovine tubercle bacilli will not grow in the complete absence of carbon dioxide and that, compared with their growth in air upon glycerine agar, air containing as low as 3 per cent carbon dioxide definitely inhibits their growth, although their viability is not appreciably affected by an exposure to this concentration of carbon dioxide in air for a period of a month. Exposure for a month to the higher concentrations of carbon dioxide, 12 per cent or more, may be said to be definitely tuberculocidal, however.

During the course of the animal experiments in which sealed and rubber stoppered tubes, small and large, containing recently inoculated cultures of tubercle bacilli upon glycerine agar were used, it was found that no growth even with a good growing laboratory strain of bacilli and a possible sufficiency of air could be obtained. This upon first consideration seemed rather peculiar, but repeated corroborating findings led to the following culture tube incubator experiment in an effort to solve or explain this fact. A large number of 8 × 1 inch heavy-walled bacteriological test tubes, containing about 15 cc. of 5 per cent glycerine agar, was divided into the following series, some seeded with tubercle bacilli, an actively growing young strain of human bacilli, and some being kept unseeded as control tubes.

Series 1. Four tubes of 5 per cent glycerine agar were sealed in the blast flame after having attained incubator temperature. The purpose of sealing the tubes only after they had attained incubator temperature was to avoid the introducton of a possible pressure factor during the period of incubation, it having been observed previously in preliminary tests that tubes containing bacilli and sealed at room temperature would not grow.

Series 2. Four tubes of 5 per cent glycerine agar were brought to incubator temperature and then were securely stoppered with a rubber stopper.

Series 3. Four tubes of 5 per cent glycerine agar were inoculated with a strain of human tubercle bacilli, capable of good growth, constricted in the blast flame, were stoppered with a paraffine cotton stopper and covered with a piece of paraffine cloth held in place by a small rubber band.

Series 4. Four tubes of 5 per cent glycerine agar were inoculated with the same strain of human tubercle bacilli as *Series 3*, were brought to incubator temperature (by residence in the incubator for a few hours), and were then glass-sealed in the blast flame with all precautions to avoid in any way injuring the bacilli or medium. The primary constricting of the tubes was carried out before the warming of the tubes to incubator temperature (this procedure was performed on all the tubes of series 3, 4, and 5) and only a small amount of heat was thus necessary to do the final sealing of this series of tubes.

Series 5. Four tubes of plain glycerine agar were inoculated with the same strain of human tubercle bacilli as *Series 3*, the tube was constricted in its upper portion in the blast flame, brought to incubator temperature, and was then securely sealed with a rubber stopper.

Thus the manipulations in this experiment were practically indentical in all the series, except that some cultures had had free access of atmospheric air and some were sealed by rubber or glass, while some tubes were inoculated and others were not.

All the tubes were then placed at incubator temperature for six weeks, after which time the cultural and carbon dioxide findings recorded in table 4 and illustrated in figures 10 to 15 were obtained. It is evident from this experiment that the carbon dioxide given off by the tubercle bacillus itself in sealed tubes can attain a concentration sufficient to inhibit even the initial macroscopic growth of the microörganism. There also seems to be a definite concentration of carbon dioxide which

TABLE 3

The effect of different gaseous concentrations of carbon dioxide upon the growth and viability of tubercle bacilli

CARBON DIOXIDE CONTENT (VOLUMETRIC) BEFORE INCUBATION	STRAINS OF TUBERCLE BACILLI	NUMBER OF CULTURE TUBES	READINGS AVERAGED AFTER				CO_2 CONTENT OF TUBES AFTER 1 MONTH INCUBATION IN PERCENTAGE VOLUMES	NUMBER OF TUBES ANALYZED AND THEN OPENED	READINGS 2 MONTHS AFTER INOCULATION 1 MONTH AFTER REMOVAL OF CO_2	
			1 week	2 weeks	3 weeks	4 weeks			Air access after removal of CO_2 †	CO_2 still retained
CO_2 free air	Human avirulent	3	–	–	–	–	0	2	+++	–
	Human virulent	6	–	–	–	–	0	3	+	–
	Bovine avirulent	3	–	–	–	–	0	2	++	–
	Bovine virulent	3	–	–	–	–	0	2	+	–
Normal air containing CO_2 (0.04 per cent)	Human avirulent	3	–	++	+++	++++	‡			++++
	Human virulent	6	–	–	±	+	‡			++
	Bovine avirulent	3	–	+	+++	++++	‡			++++
	Bovine virulent	3	–	+	++	++++	‡			++++
3 per cent CO_2 in air	Human avirulent	3	–	–	+	+	3.0*	2	+++	++
	Human virulent	6	–	–	–	–	2.5	3	+++	++
	Bovine avirulent	3	–	+	+	++	3.0	2	++++	+
	Bovine virulent	3	–	–	+	+	3.0	2	+++	+
6 per cent CO_2 in air	Human avirulent	3	–	–	–	–	6.0	2	++++	–
	Human virulent	6	–	–	–	–	5.6	3	–	–
	Bovine avirulent	3	–	–	–	–	6.0	2	+++	+
	Bovine virulent	3	–		–	–	5.5	2	++	–
9 per cent CO_2 in air	Human avirulent	3	–	–	–	–	8.5	2	+	–
	Human virulent	6	–	–	–	–	7.0	3	–	–
	Bovine avirulent	3	–	–	–	–	9.0	2	+++	–
	Bovine virulent	3	–	–	–	–	7.5	2	++	–

12 per cent CO_2 in air.......	Human avirulent	3	—	—	—	—	11.5	2	—	—
	Human virulent	6	—	—	—	—	11.0	3	—	—
	Bovine avirulent	3	—	—	—	—	12.0	2	—	—
	Bovine virulent	3	—	—	—	—	12.0	2	+	—
15 per cent CO_2 in air.......	Human avirulent	3	—	—	—	—	14.5	2	+	—
	Human virulent	6	—	—	—	—	14.3	3	—	—
	Bovine avirulent	3	—	—	—	—	15.0	2	—	—
	Bovine virulent	3	—	—	—	—	14.5	2	+	—
30 per cent CO_2 in air.......	Human avirulent	3	—	—	—	—	28.0	2	—	—
	Human virulent	6	—	—	—	—	30.0	3	—	—
	Bovine avirulent	3	—	—	—	—	24.0	2	—	—
	Bovine virulent	3	—	—	—	—	22.0	2	—	—
Pure CO_2..................	Human avirulent	3	—	—	—	—	55.0	2	—	—
	Human virulent	6	—	—	—	—	60.0	3	—	—
	Bovine avirulent	3	—	—	—	—	50.0	2	—	—
	Bovine virulent	3	—	—	—	—	68.0	2	—	—

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* The figures in this column are the average obtained from all the tubes analyzed in each set.

† Rubber stoppers were removed for one hour to permit escape of carbon dioxide and tubes were then stoppered with paraffine cotton plugs.

‡ No analyses.

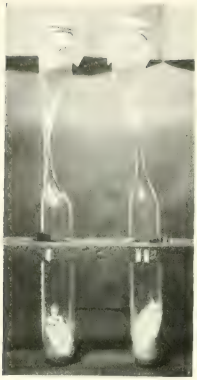

FIG. 10

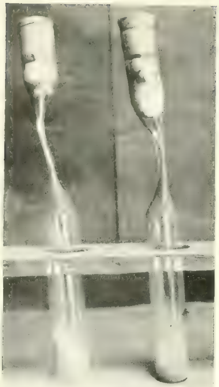

FIG. 12

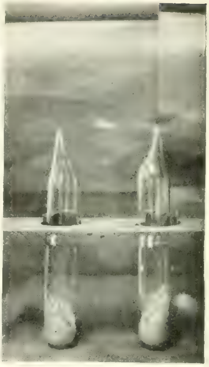

FIG. 14

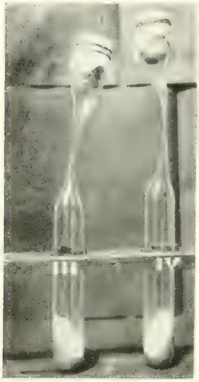

FIG. 11

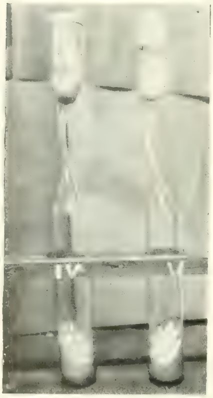

FIG. 13

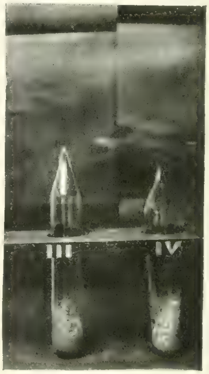

FIG. 15

FIGS. 10 TO 15. GROWTH OF HUMAN TUBERCLE BACILLI ON GLYCERINE AGAR IN TUBES OPEN TO ATMOSPHERIC AIR AND SEALED

FIGS. 10 AND 11. *Atmospheric air series.* Growth in four tubes containing glycerine agar, drawn out in the blast flame after inoculation, stoppered with paraffined cotton and covered with paraffined cloth, after six weeks at 37.5°C.

FIGS. 12 AND 13. *Sealed with rubber stoppers.* Four tubes, containing glycerine agar, drawn out in the blast flame after inoculation, closed with rubber stoppers after reaching 37.5°C., and incubated at this temperature for six weeks. Analyses for carbon dioxide at the end of this time revealed the presence of about 5 to 6 per cent by volume. Tubes II and V show growth.

FIGS. 14 AND 15. *Glass sealed tubes.* Four tubes, containing glycerine agar, sealed in the blast flame after inoculation and reaching 37.5°C., and incubated at 37.5°C. for six weeks. Analyses revealed about 5 to 6 per cent carbon dioxide by volume. There is an entire absence of growth in all four tubes, which were heavily seeded to ensure ample opportunity for growth and show only the original clumps of bacilli.

can be attained in the sealed tubes and which lies at about the 5 per cent volume concentration, at which all metabolic activity of the tubercle bacillus ceases. If the tubes are sealed by a substance slowly absorbing carbon dioxide, as was pointed out to be the case with rubber by Haldane, the culture can attain a considerable visible growth before the concentration of carbon dioxide becomes sufficiently high to stop the growth (see figures 10 to 15).

THE EFFECT OF THE BODY GASES UPON THE GROWTH OF THE TUBERCLE BACILLUS

In order to study the influence of the gases of the body upon tubercle bacilli under control the following experiments were performed:

Since the gases of the body contain about 6 per cent carbon dioxide, it was reasoned from the *in vitro* experiments with carbon dioxide that culture tubes appropriately prepared to allow easy access of these gases should show a definite inhibition of the growth of the tubercle bacilli.

In the early part of the animal experiments, tubes of glycerine agar seeded with tubercle bacilli were placed in the peritoneal cavity, part of them glass-sealed for controls and part of them stoppered with sterile glass wool, to keep the body fluids out, and with a two-hole rubber stopper to aid in preventing an influx of these fluids. It was soon learned, however, that growth did not occur in either the sealed or the open tubes. In other words, the glass-sealed tube did not prove to be a control as was hoped. It was, therefore, necessary, first, to devise a method for growing the tubercle bacillus in the animal body which could serve as control.

After a great many trials the best success was obtained with a large 6 × 1 inch heavy-walled bacteriological test tube, which contained a slant of 5 per cent glycerine agar, seeded with a young actively growing strain of human tubercle bacilli. This tube was constricted in the blast flame about three inches above the agar slant, to a diameter of about $\frac{1}{4}$ to $\frac{3}{8}$ of an inch and with the open end flared out. The constricted top of the tube was stoppered with sterile cotton and into this was dropped sterile melted paraffine, not to saturation, however. The top of the tube was then sterilized by gently heating in the flame, while the bottom of the tube containing the culture medium and bacilli was sterilized by immersion for five minutes in 90 per cent phenol in 95 per cent alcohol, the phenol being subsequently removed by rinsing in sterile 95 per cent alcohol, the excess of alcohol drained off, and the remainder quickly burned off without, however, permitting the contents of the tube to become more than slightly warm. The tube, thus sterilized, was placed in a sterile light-proof container and kept (not more than a few days) until it was inserted into the subcutaneous tissues of the back of the dog. An incision about one to two inches was made into the skin, slightly to the right or left of the midline of the back. By blunt dissection a pocket was made subcutaneously, sufficiently large to hold the culture tube. Those tubes to have access to atmospheric air were inserted into this pocket and a small hole was made about three inches lateral to the original incision, just large enough to permit the mouth of the culture tube to pass out. Thus the tube was kept away from the primary incision. The tube was then held in place by means of loops of sterile silkworm gut, around the neck and just anterior to the place where the tube had been drawn out.

TABLE 4

The growth of human tubercle bacilli in tubes sealed and closed with paraffine cotton stoppers

METHOD OF SEALING TUBE	NUMBER OF TUBE	CULTURAL RESULT SIX WEEKS AFTER BEGINNING EXPERIMENT	CARBON DIOXIDE CONTENT IN PER CENT BY VOLUME AFTER 6 WEEKS AT 37.5°C.	
			Inoculated tubes	Uninoculated controls
Paraffine cotton stoppered	1	+++*	Atmospheric air	Atmospheric air
	2	+++	Atmospheric air	Atmospheric air
	3	+++	Atmospheric air	Atmospheric air
	4	+++	Atmospheric air	Atmospheric air
Closed with rubber stopper at incubator temperature	1	+++	Atmospheric air	Atmospheric air
	2	++	5.2†	Atmospheric air
	3	—	5.5	Atmospheric air
	4	—	5.2	Atmospheric air
Glass sealed at incubator temperature	1	—	4.7	Atmospheric air
	2	—	5.2	Atmospheric air
	3	—	5.5	Atmospheric air
	4	—	5.5	Atmospheric air

Note: All the tubes were heavily seeded with human tubercle bacilli from a young actively growing laboratory culture about six weeks old.

* The amount of growth obtained at the end of six weeks at incubator temperature is graded from —, the amount originally planted on the medium, to +++, a luxuriant growth.

† These figures are the average of four analyses for carbon dioxide made of the gas from the same culture tube. The tubes never analyzed less than 4 per cent or greater than 6 per cent carbon dioxide by the method of analysis employed.

The operations were performed under ether anesthesia and absolutely aseptic precautions.

The buried tubes were prepared similarly to the open tubes, except without the flanged end, with paraffine cotton stopper and sterilized; but they were inserted into the subcutaneous pocket open end first, so that they would be completely buried in the tissues. To hold the tubes in place and away from the incision, stay sutures of silkworm gut were used, just constricting the bluntly dissected pocket. In all cases the primary incision thus usually healed early and the skin stitches could be removed in from five to seven days. The stay sutures were not removed until the culture tubes were taken out at the end of the experiment. The tubes were allowed to remain subcutaneously for about four to six weeks, when comparison could be made. All the dogs were kept in dark cages during the course of the experiment, to rule out any detrimental influence of light upon the cultures. Thus the one set of tubes with external opening and access to atmospheric air were incubated in the animal body, while the buried tubes were incubated at body temperature and exposed to the tissue gases.

Accidents encountered in these experiments were fairly common and included a sloughing out of the tubes before termination of the experiment, which occurred only in those with external opening; a shaking up of the culture medium; breaking off of the tip of the tube; and an infection of the pocket with accumulation of fluid, which would flow into and spoil the buried tubes especially. In spite of these difficulties a great many experiments came to term without mishap.

About fifty dogs were used in this part of the studies, while in the studies in which tubes were buried intraperitoneally there were about twenty-eight dogs. In many of the latter, however, two to three tubes were buried in the same animal, while in the subcutaneous studies each animal received only one tube. In all the animal experiments, however, which terminated without mishap, entirely consistent results were obtained. There was never a growth of the tubercle bacilli in any of the buried tubes, exposed to the tissue gases even after eight weeks, whereas in all of the exposed tubes, into which easy access of atmospheric air was allowed through the paraffined cotton stopper, a good growth was obtained within four to six weeks (see figures 16 and 17).

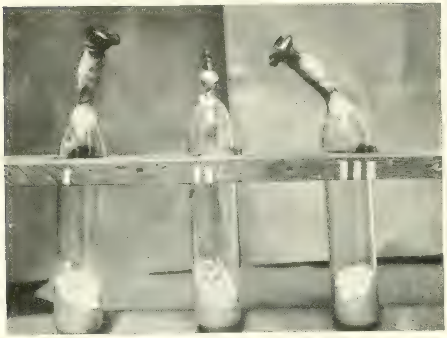

FIG. 16

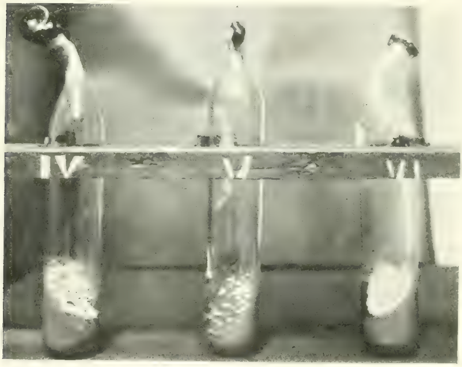

FIG. 17

FIGS. 16 AND 17. A COMPARISON OF THE GROWTH OF TUBERCLE BACILLI UPON GLYCERINE AGAR INCUBATED IN THE SUBCUTANEOUS TISSUES AND EXPOSED TO ATMOSPHERIC AIR OR TISSUE GASES

Tubes I, III, IV and VI were buried in the subcutaneous tissues of the back with the upper, open end exposed to atmospheric air for six weeks. They show profuse growths.

Tubes II and V were completely buried in the subcutaneous tissues. The upper, open ends were thus exposed only to tissue gases. The tubes were heavily seeded and show entire absence of growth.

THE CARBON DIOXIDE CONTENT OF TUBES BURIED IN THE SUBCUTANEOUS TISSUES

Since it was determined that the cultures of tubercle bacilli, buried in the tissues of dogs and permitted to acquire the carbon dioxide concentration of the body, were inhibited, it seemed desirable to determine further the approximate carbon dioxide concentration of such buried tubes, and how soon, after being put into the subcutaneous tissues, the maximum concentration would be attained under the conditions of experiment used above. For this purpose a set of tubes was prepared that were stoppered with a firm paraffine cotton plug as above, and sterile but empty, except for the presence of atmospheric air. There was also a second set identical to the first but containing a slant of 10 cc. of sterile 5 per cent glycerine agar, and a third set similar to the second but planted with human tubercle bacilli. One each of these tubes of the three sets was inserted into the subcutaneous tissues of the back of a dog with the open end distal to the incision, the technique being similar to that used in the above animal experiments; and at certain intervals the three tubes from one dog were removed, using all possible

TABLE 5

The carbon dioxide content of culture tubes buried in the subcutaneous tissues after certain intervals

DESCRIPTION OF TUBE[*]	PERIOD OF TIME IN HOURS DURING WHICH TUBES WERE BURIED BEFORE ANALYSIS FOR CARBON DIOXIDE CONTENT						
	1.5	3	6	24	48	72	144
	per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
Empty sterile test tube stoppered with paraffine-cotton	2.0[†]	1.3	1.7	2.7	4.7	5.0	—
Sterile tube containing a slant of 5 per cent glycerine agar stoppered with paraffine-cotton	Lost[‡]	1.7	2.0	2.3	5.0	Lost	4.7
Sterile tube containing a slant of 5 per cent glycerine agar inoculated with human tubercle bacilli and stoppered with paraffine-cotton	1.3	Lost	Lost	2.7	5.3	4.7	—

[*] The three tubes listed below this heading were inserted subcutaneously in one dog for each different time interval, making a total of seven dogs used in this experiment.

[†] The figures given are the results of the average findings of three analyses for carbon dioxide content by volume of the gas from one tube.

[‡] *Lost* indicates that through error in manipulation for analysis the entire tube was lost for accurate determination of its carbon dioxide content.

precautions to avoid gaseous loss while placing the tubes over mercury for subsequent analysis. The gases of the tubes were then carefully analyzed for carbon dioxide with the results given in table 5.

An examination of table 5 reveals that the carbon dioxide content of the paraffine-cotton stoppered tubes placed in the subcutaneous tissues of the dog gradually increases until it reaches its maximum of about 5 per cent after forty-eight hours, which is then maintained.

SUMMARY AND CONCLUSIONS

Humoral antibodies have failed to explain resistance to tuberculosis, the lymphocyte as the important factor is rapidly being discarded, allergic phenomena require further elucidation, and the phagocytic action of the wandering cell is recognized as important. But both humoral and cellular mechanisms of resistance leave much to be explained.

Weber's empiric reasoning that the deficiency of carbon dioxide in the body favors tuberculosis, while an accumulation retards the progress of the disease, seems to be highly significant, but his disregard of laboratory procedures precluded his crystallizing the conception, in so far as it deprived him of the specific data essential to substantiate his theories. Further, it led him into some crude basic biochemical blunders. However, his main empirically reasoned principles appear to be substantiated by our experimental work.

We have observed that 3 per cent carbon dioxide causes some inhibition of the growth of the tubercle bacillus in the test tube and that 15 per cent is tuberculocidal. Tubercle bacilli will not grow in a carbon dioxide-free atmosphere.

Cultures of tubercle bacilli buried in the tissues of animals and permitted to acquire the carbon dioxide concentration of the body are definitely inhibited in their growth, while other cultures similarly buried, except that ingress of atmospheric air is permitted, show no inhibition.

When viable tubercle bacilli are placed in a closed system, their growth becomes inhibited as the carbon dioxide which the organisms elaborate approaches a concentration of approximately 5.5 per cent; at which concentration respiration of these microörganisms is also reduced to a minimum. In a closed system the end products of metabolism automatically inhibit the growth of the organisms that give rise to them. This, of course, holds true in a measure for all biological growth phenomena, namely, that the end products of metabolism if permitted to accumulate will attain a concentration at which they become toxic to the organisms elaborating them and consequently inhibit their growth and later may even destroy them.

The significant feature of this study with the tubercle bacillus is that the concentration sufficient to inhibit definitely its growth, namely 5.5 per cent, occurs normally in the human body; and the experiments conducted both in the test tube and in the animal body indicate that this concentration actually does inhibit the growth of the tubercle bacillus.

It appears, therefore, that this factor is extremely significant in the rôle of resistance to tuberculous infection and the subsequent development of the disease in the body; further that the normal body apparently possesses, by virtue of containing sufficient carbon dioxide, the ability to inhibit the growth of the tubercle bacillus. Experiments are now in progress to study further phases of this problem.

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AN X-RAY STUDY OF THE PROGRESSIVE CHANGES IN THE LUNGS AND AORTA IN TUBERCULOSIS WITH SYPHILIS

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From the Clinic of the Boston Consumptive Hospital, Boston, Massachusetts

The advance of pulmonary tuberculosis may be followed clinically by means of the stethoscope, with X-ray plates, or summed up by the pathologist from a study of the age and character of the lung lesions. The progressive changes in the lung tissue are known to be due to the involvement of the finer lymph spaces and bronchioles with tuberculous material and the coalescence of these into areas of tuberculous tissue.

The clinical course of the disease commonly observed is the involvement of one apex, the extension of the process throughout the lobe and then the appearance of the disease in the opposite apex.

Often, after the disease has advanced to a certain extent in one lung, it may become quiet or even healed, while in the opposite lung there may be steady progress. The changes noted in the case of bilateral fibroid disease are much less marked and take place much more slowly than in the case of an acutely active process. The course of the disease, as it progresses, is shown more through its effect upon other organs than the lungs. The pulmonary changes are those of infiltration and retraction of tissue. The full extent of pulmonary involvement is almost never apparent on clinical examination alone. The X-ray plate demonstrates scattered tubercles well beyond the border of clinical signs. Often, where the chest signs are confined to the upper half of a lobe, tubercles may have occurred throughout the lung. This method therefore offers the opportunity of a systematic survey of the pulmonary tissue. The same is true in syphilitic lesions of the aorta. The aneurysmal dilatation in syphilis may be followed, step by step, in its course; and the effect of treatment can be readily observed. For detection of pulmonary syphilis the X-ray is a valuable adjunct, as few of these lesions come to autopsy and the condition must be demonstrated by clinical methods.

The pulmonary lesions of syphilis are still under discussion and there are wide differences of opinion as to what constitutes them. Funk well emphasizes the fact that the failure to recognize luetic bronchitis in the second stage of the disease has frequently led to the diagnosis of phthisis. It is, however, in the old obscure case of syphilis, where the disease has been overlooked for years, that we may expect to find pulmonary involvement.

Pulmonary syphilis, as it is known clinically, consists of a symptom complex of history, positive Wassermann test, extrapulmonary lesions, continued negative sputum for the tubercle bacillus and pulmonary signs found at the base or toward the hilum.

Dunham suggests that those lesions giving rise to clinical signs in the lungs, but negative by the X-ray, are probably syphilitic. There is a general belief that pulmonary syphilis occurs as a basal lesion or as a gummatous mass near the hilum.

The observations of Hoffman, Tenueka, Landis and others show that an apical process may occur quite as frequently as one at the base. When an isolated area of infiltration occurs at the hilum or base, syphilis will be at once suspected; but where the lesion is an apical one, or occurs coincident with tuberculosis, only the effect of prolonged syphilitic treatment will give a clue to the real character of the disease.

The X-ray picture of pulmonary syphilis is not one to allow of certainty as to the condition present. The irregularity of outline, indefinite shape and moderate density of the process in the lung, are the positive points in favor of this diagnosis.

The effect of syphilis on the aortic arch is well recognized; but the results of treatment after the lesion is established are still under discussion. Involvement occurs as an early manifestation and may progress to a neurysmal dilatation.

All grades of the process occur from a slight localized broadening of the shadow to a dilatation of the aorta with cardiac enlargement due to aorta regurgitation.

The effect of an intercurrent syphilitic infection upon an established pulmonary tuberculosis is that of stimulation of the production of fibroid tissue formation. How far this tendency may aid in preventing the condition of cavitation of the lung is uncertain.

The procedure of a routine Wassermann test in the clinic of the Boston Consumptive Hospital has shown that 8 per cent of the male patients have syphilis. Fifty of these cases have been followed by physical and

X-ray examinations over a period of years, during which time they have been treated more or less intensively for syphilis. There have appeared only two cases that were fairly typical of pulmonary syphilis, although several lesions in mixed infections of the lung receded under treatment where the pleura or the lungs were involved. In several cases clinical signs were present where the X-ray plate was negative, suggesting, according to Dunham, a luetic lesion. In three instances the appearance of the beginning formation of a cavity was obtained by the X-ray, which a year later had entirely disappeared and homogeneous fibroid tissue was alone in evidence.

Observations of the effect of syphilis upon the aorta show the great frequency with which it is affected. The progressive dilatation of the arch has been observed to follow more or less closely the intensity and extent of the treatment. Where it has been intensive, we have frequently noted a definite diminution of the size of the arch and a secondary effect upon the heart. If the treatment is neglected or is irregular, the lesion advances to a point when no results are obtainable. Even an aorta giving a shadow of 3½ inches in diameter may respond under treatment and show a diminution in the shadow.

CONCLUSIONS

1. Every case having tuberculosis and syphilis combined should be given intensive syphilitic treatment, more especially if the lesion is not typically one of tuberculosis.

2. The presence of syphilis may at times considerably aid in the production of fibrous tissue in the lung.

3. Syphilitic dilatation of the aortic arch, even in well marked instances may be improved by prolonged intensive antisyphilitic treatment.

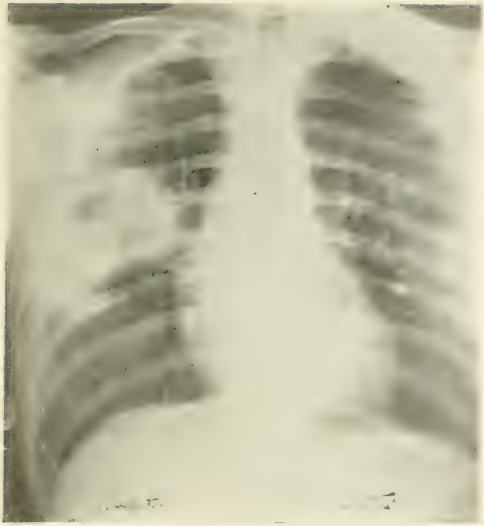

Fig. 1

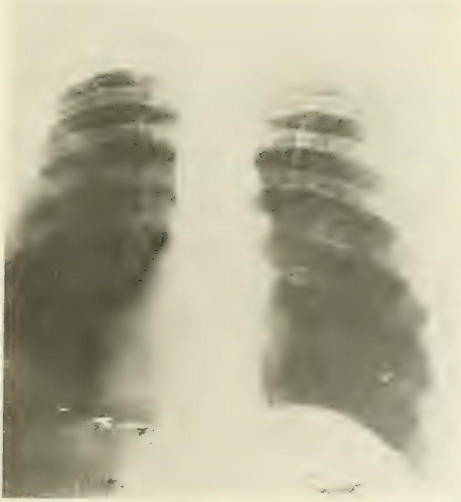

Fig. 2

Figs. 1 and 2. X-Ray Pictures of a Patient with a Positive Wassermann Test Treated for Syphilis

Fig. 1. April, 1917, showing a circumscribed area of infiltration in the right middle lobe spread out in fan shape fashion from the root of the right lung.

Fig. 2. April, 1920. Shadow in right middle lobe has entirely disappeared. Heart and lungs negative.

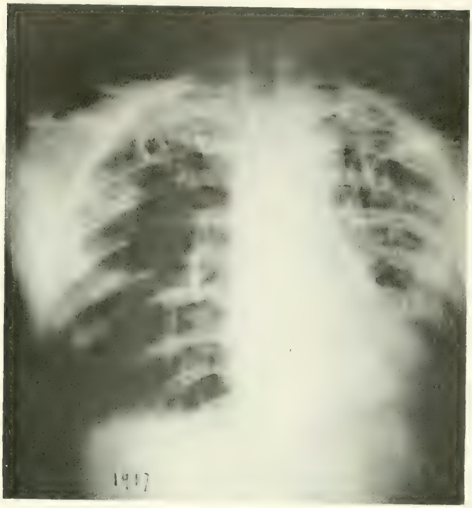

Fig. 3

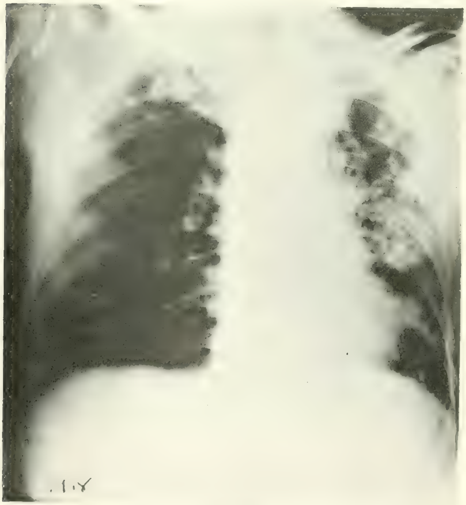

Fig. 4

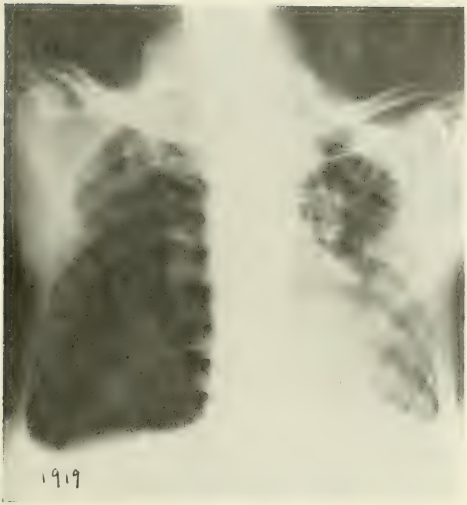

FIG. 5

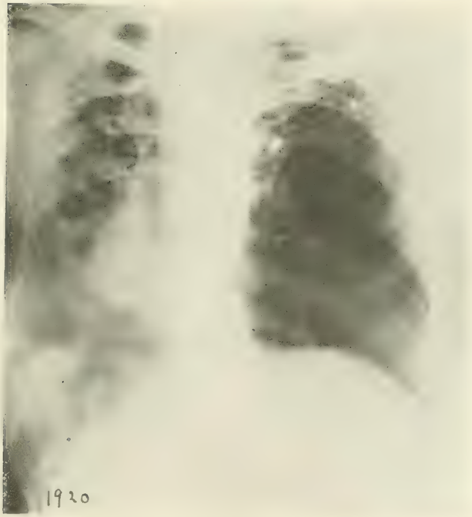

FIG. 6

FIGS. 3, 4, 5 AND 6. X-RAY PRINTS OF A PATIENT WITH PHTHISIS HAVING A POSITIVE WASSERMANN TEST

Four observations—1917: Tuberculosis of both upper lobes. During 1918–1919 process on the right became fibroid and also less extensive. During 1919–1920 the left sided process extended to the base by pleural involvement. The aortic arch showed some dilatation in 1917, which was less marked in 1920. The interesting feature is the diminution of the signs on the right under antisyphilitic treatment.

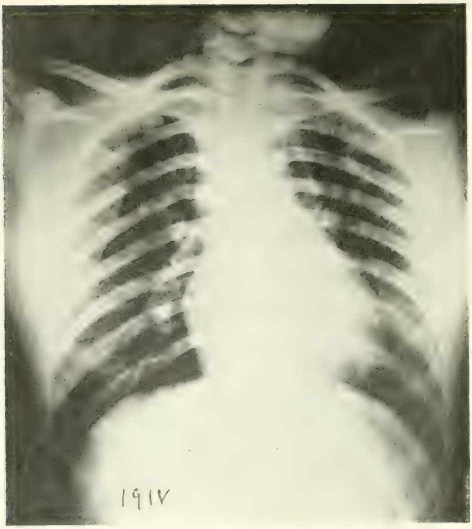

Fig. 7

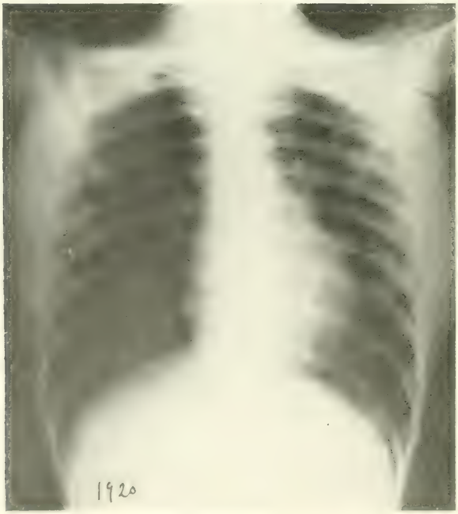

Fig. 8

Figs. 7 and 8. X-Ray Prints of a Patient with Tuberculosis of the Left Apex, Positive Wassermann Test and an Aorta Increased in Size

Under treatment the aortic base returned to normal dimensions in two years time

SMALLPOX VACCINATION AND PULMONARY TUBERCULOSIS

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Reports concerning the increasing incidence of smallpox in the United States have come from various localities. A number of cases having been discovered recently in southwestern Virginia, it seemed wise to guard against the possibility of an epidemic breaking out at our sanatorium, by vaccinating all patients and employees who had not been vaccinated successfully within the last five years. This decision was concurred in by the Commissioner of Health. On making a survey of our patients with a view of selecting those for vaccination it was found that 21 or 18.5 per cent of the existing census of 113, had never been vaccinated. A total of 93 patients were included in the list for vaccination. Twenty infirmary patients who were running high temperatures were omitted.

There is a paucity of observations on vaccination and vaccinia in the course of active tuberculosis; and, while this communication must of necessity be in the nature of a preliminary report, we feel that it is of sufficient importance at this moment, when on account of neglect of vaccination there is a material increase of smallpox in the country at large. The routine vaccination of patients and employees in public institutions acquires a greater significance, therefore, and our own experience may be of help to physicians in charge of tuberculosis hospitals and sanatoriums, who might hesitate to carry out vaccination in active cases for fear of aggravating pulmonary lesions through possible febrile reactions. In this connection we would refer to Howk and Lawson's experience at the Metropolitan Life Insurance Sanatorium, which was reported last year (1), and which offered us considerable moral support in issuing a general order for routine vaccination, as many of the cases were not only active but far advanced; and we might have hesitated in taking such a step for fear of setting up severe focal reactions or causing extensions of tuberculous lesions. However, a study of this first group of cases, a month after vaccination, would indicate that our experience agrees with that of Howk and Lawson, namely, that vaccinia, even if accompanied by quite severe clinical and constitutional symptoms, is only transitory and does not have any discoverable effect on tuberculous lesions so far as can be ascertained by physical examination.

All vaccinated patients had had the usual routine chest examination within a short time before vaccination and were kept in bed during the active manifestations of vaccinia, if there were any febrile reactions of 100° F. or more. They were given a special and very careful examination after all local and general symptoms of vaccinia had subsided. In only one of them was there any increase in the number of râles, but in this case the disease had been progressing for sometime. In only one patient was a serial X-ray plate made after vaccination, and this showed less density of rather circumscribed shadows than the last previous one. This confirmed the signs obtained on physical examination. This case had had a positive sputum examination on several occasions before vaccination, but several repeated direct examinations of the sputum since vaccination have been negative. In this case, a second vaccination, in a young girl twelve years of age, the symptoms of vaccinia had been mild with a maximum temperature of 99.8°. In one chronic fibroid case with considerable activity, referred to above, a man fifty-six years of age (first vaccination), the subjective and local symptoms of vaccinia were more severe than the average and lasted for ten days. There was a maximum temperature of 102°F., occurring on the eighth day. This was the case in which the local signs in the lungs had apparently been more marked. However, as soon as the vaccinia had subsided the patient maintained that he felt better than he had before. His appetite was increased and he gained in weight, whereas he had remained stationary for some months before. As shown by the accompanying table there were a number of cases with severe vaccinia, but once the symptoms had subsided most of the patients stated that they felt better than they had before vaccination. Needless to say, the writers do not wish to give the impression that there was any real therapeutic value in vaccination, and cite these statements simply as the hearsay evidence of patients regarding their subjective symptoms.

The period of incubation varied from five to ten days and the average duration was about four days. The highest temperature recorded was 104°, which continued for several days. In a group of 19 employees, all of them colored, two of whom had never been vaccinated before, the symptoms of vaccinia were as severe as in the patients with active tuberculosis. The vaccine used was from the same source and the same method of technique was employed. These cases might serve as controls, showing apparently that the tuberculous process in itself did not influence the severity of the vaccinia.

The table shows the distribution of tuberculous cases, vaccinated according to the classification, and the effects of vaccination in each group. From these figures it would not appear that the stage of tuberculosis had determined any difference in the severity of the vaccinia. These figures agree moreover with the impressions obtained from an individual study of the cases which cannot be presented accurately without going into a detailed description of each case.

TABLE 1

The results of vaccination in 93 tuberculous patients. All primary vaccinations were positive. Severe vaccinia noted only in primary vaccinations. Vaccinia as severe in early cases as in far advanced. Moderately advanced cases showed severe vaccinia in approximately half the cases.

CLASSIFICATION OF PULMONARY CONDITION (NAT. TUB. ASS'N)	RESULTS OF VACCINATION				PULMONARY CONDITION ONE MONTH AFTER VACCINATION	
	Primary		Secondary			
	Positive	Negative	Positive	Negative	Changed	Unchanged
Minimal, 23 cases	6 (All severe vaccinia)	0	2	15	0	23
Moderately advanced, 62 cases	11 (5 severe vaccinia)	0	9	42	0	62
Far advanced, 8 cases	2 (Both severe vaccinia)	0	1	5	1 Increased activity	7
Totals, 93 cases	19	0	12	62	1	92

Summing up briefly, it would appear from our observations that vaccination is not contraindicated in tuberculosis and does not exert any unfavorable influence on tuberculous processes in the lungs.

It would be proper to conclude, therefore, that routine vaccination is not only a safe procedure, but rather a necessary safeguard in connection with tuberculosis sanatoriums, in view of the increasing incidence of smallpox in many parts of the United States.

It is safe to state that vaccinia is at least less severe than smallpox. There can be no question but that in the case of many large tuberculosis institutions, which are not planned to provide for proper isolation and treatment of acute infectious diseases, an epidemic of smallpox would prove a serious administrative problem and an emergency difficult to meet, comparable only to a large conflagration. Assuming that the proportion of unvaccinated in other communities is as large as it was in our own, such an occurrence might not be so remote a possibility.

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PURULENT EFFUSIONS COMPLICATING ARTIFICIAL PNEUMOTHORAX[1]

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It is granted by tuberculosis workers, especially those doing a great deal of artificial pneumothorax, that effusions of a serofibrinous character are found sooner or later in the majority of their patients. Later on, a small percentage of such effusions become purulent, and finally a still smaller percentage become true empyemas.

It is generally granted that tuberculous pleurisies are in a class by themselves, and admitted that the purulent effusions may be primary, or may occur secondarily to the serofibrinous form. It is also granted that these purulent effusions are sterile, except for the presence of the tubercle bacillus and further, that in the very beginning the cell count will show a high percentage of polynuclears, but later, as the effusion develops, the lymphocyte will be the predominating leucocyte.

The point I wish to emphasize is the occurrence of purulent effusions in tuberculosis without the ordinary pus organisms such as the staphylococcus, pneumococcus or streptococcus.

In the gas cases the occurrence of purulent effusion, usually secondary to the serofibrinous variety, is possibly more common than in the non-gas cases. This I believe is due to the ease with which the tubercle is allowed to spread. In a noncompressed lung the eruption of tubercle is a limited process due to the apposition of the pleural surfaces, while in the compressed lung no such apposition occurs. Thus, an extensive surface offers an unlimited field for the eruption of tubercle and the flooding of the effusion with countless bacilli.

The formation of effusions in gas cases bears no striking difference in symptoms to the formation of fluid following a pleurisy.

There is usually a sudden onset, sometimes with a distinct chill, followed by chilly sensations for days and high fever, 102°-104°, with marked prostration in many patients. Usually after a few days, the presence of fluid can be determined, although in a compressed lung it is much more difficult than in a normal chest, unless one has access to the fluoroscope when minute quantities can be detected. The fever gradually subsides, and at the end of two or three weeks will usually be normal.

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[1] Read before the Southwestern Medical and Surgical Assocation, December 12, 1920.

The treatment in the gas cases is one of watchful waiting. Unless the fluid reaches such a volume as to cause pressure symptoms, it had better be left alone, for it acts as a means of compression, and one need not disturb the patient with injections of air during the height of the fever. It has been my experience that the removal of fluid will have little effect on the fever any way, and re-accumulation will take place rapidly—sometimes in twenty-four hours. It is surprising what amounts a chest will hold without pressure symptoms. This in part is due no doubt to the fact that the lung has been compressed over varying periods of time and the patient is not conscious of a sudden compression due to a rapid accumulation of fluid.

I have now been using lung compression for eight years, and have attempted an artificial pneumothorax in 250 patients. In this number, I have had 26 cases of purulent effusion. In all these cases, examination of the fluid by smears has been made and cultures planted. Eight of these have shown mixed infection pus and the remaining 18 have proved negative; in other words, showing only the tubercle bacillus.

In the eight empyemas, drainage was done and the ultimate outcome was death in six. One obtained a perfect healing at the end of a year and lived in excellent health for four years, working during that time, when a recurrence was noted and death followed a second operation. The one other is still alive, having fallen into the hands of another physician who advised rib resection. A radical operation was done cutting out the ribs from the second to the ninth. He is still alive, but the prognosis is hopeless.

All the remaining 18 cases showing sterile pus made recoveries from the initial fluid formation and continued their treatment. Out of that number, I was able to follow the subsequent history of ten. Twoof these died from terminal tuberculosis, the opposite lung becoming extremely involved. One died from kidney and heart complications, due no doubt to toxic absorption over a long period of time; and one is still living, although recently sent home with a hopeless prognosis.

Four have carried more or less pus for the past three years, but have been in good health. One of these practices law, one is an artist and works daily, one is employed in a clerical position, and one keeps house for a large family. The other two are still under treatment, but doing well.

In passing I may say that the true empyemas are usually caused by spontaneous pneumothorax. This I was able to demonstrate in 6 of the 8 cases reported, and I am sure the other 2 are of the same nature, although the physical findings could not warrant such a diagnosis.

From the foregoing let me draw the following conclusions:

1. Purulent effusions, due only to the tubercle bacillus, are found in tuberculous pleurisies independent of artificial pneumothorax. These may be primary or secondary to a serofibrinous effusion.
2. Many of these effusions may in the beginning show a high percentage of polymorphonuclears. Later, as the effusion develops, the lymphocytes predominate.
3. The formation of fluid in the "gas chest" is identical with the formation of fluid in the average tuberculous pleurisy, giving rise to the same symptoms, but the purulent effusion is perhaps more often noted in lung compression than elsewhere.
4. Treatment is expectant. Removal of fluid should be performed only when necessary to relieve pressure symptoms.
5. The average patient with sterile pus recovers as easily and as quickly as the average patient with only a serofibrinous effusion.
6. True empyemas must be treated by drainage and their prognosis is usually hopeless.

THE RÔLE OF THE INTERNATIONAL UNION IN COMBATING TUBERCULOSIS[1]

GEORGE E. BUSHNELL

There can be of course no question but that the diagnosis, treatment and prophylaxis of tuberculosis, as well as the education of the people in practical prophylaxis, all depend ultimately upon our conceptions of the pathology of the disease. It is, therefore, unfortunate that notwithstanding an enormous amount of work and many notable advances in our knowledge, the views held as to the pathology of tuberculosis are as discordant as ever. Little real progress can be made until we agree better as to the fundamental questions of tuberculosis.

Why does this discordance exist? Largely, it seems to me, because of the neglect of fundamentals for the study of other questions of a more advanced and recondite nature. It is to the importance of the study of these fundamentals in tuberculosis that I desire to invite your attention.

When the discovery of the tubercle bacillus furnished for the first time simple and objective criteria for the detection of tuberculosis in its manifest forms, the tuberculous stood out as a well marked class, sharply distinguished from the healthy. On one side of the line in our conception were the tuberculous who were to be shunned as sources of infection; on the other side of the line stood the healthy who were to be protected against the disease by ordinances and regulations, no matter how oppressive to the tuberculous members of the community. But difficulties at once arose in applying in practice this simple classification. The disease is insidious; some who seemed healthy proved to be its victims. The task that confronted the profession was the detection of masked tuberculosis. The line that had seemed so sharp now proved to be sometimes obscure and confused. But greater difficulties impended.

The introduction by von Pirquet of the cutaneous tuberculin test was only less important from an epidemiological standpoint than the discovery of the tubercle bacillus. We remember the consternation with which the medical profession received the demonstration that at least a very considerable portion of the supposedly healthy members of the civilized community had come into contact with the tubercle bacillus to the point of reacting to tuberculin, and were therefore properly to be considered as infected with tuberculosis. The medical men of the United States at least averted their eyes from the idea as from a spectacle too terrible to witness. Every effort was made to minimize the importance of the unwelcome revelations. The positive findings were obtained, it was said, among the proletariat of European cities; they did not apply to the conditions of American life. An attenuated tuberculin gave us much smaller percentages in the cutaneous test than those of Vienna, and we derived consolation from the fact. But the old line of demarcation between the well and the tuberculous had lost its value—too many of us belonged on the wrong side of the line. The distinction was soon made between tuberculous infection and tuberculous disease, and the line was now drawn between these two conditions.

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[1] An address delivered at the meeting of the International Union Against Tuberculosis, London, England, July 26, 1921.

Now the theoretical distinction between those who need treatment and those who do not is simple enough. The difficulty in practice is to determine who it is that requires treatment. Newly discovered methods of employing tuberculosis antigens seemed to promise aid, and many efforts have been made so to use tuberculin that it should detect tuberculous disease and not confound the results by indicating also what is only tuberculous infection. Laboratory workers also have exhausted their ingenuity in devising combinations of antigens which should reach the same end through the complement binding reaction. I need not add that these various endeavors have as yet proved fruitless, the reason for this being that a sharp line of distinction between infected individuals who have and who have not an active tuberculosis does not exist. The reactivity of the individual only, not his need of treatment, is indicated by such tests.

We have, therefore, felt compelled to continue to place our dependence upon physical diagnosis, in order to distinguish between tuberculous infection and tuberculous disease. We are not, I think, altogether satisfied with the results that we obtain, yet in no other disease is the diagnosis so accurate as to details. In few other diseases is it even attempted to make a topical diagnosis, to determine past history and to follow the course of the morbid process from month to month in the various portions of a single organ. We can do so much because of the extraordinary variety and delicacy of the signs furnished to us by the lungs. We command many resources; is it not a fair question whether we make full use of them all? If I may be permitted a suggestion, I would say that our difficulties often arise from a too narrow view. The tuberculous lesion, as we find it outside of the period of infancy, is rarely the primitive lesion and is only to be comprehended fully when we regard it as constituting one of the chapters of a perhaps long history. Some of the chapters of this prolonged record have been but little read. It is our ignorance of these chapters which should by all means be remedied.

Because of the assumption that the tuberculous lesion found, we will say, in the apex is the sole expression of the tuberculosis, that it is recent because recently discovered and that it is active because recent, we are in danger of laying too much stress upon incipiency and too often confound the incipient lesion with the obsolete. We, as clinicians, do not always give due weight to the fact that the X-ray usually shows the existence of a deep tuberculosis—a chapter in the history of the disease which is sealed to us, so far as practical application of our knowledge is concerned. We practically ignore, as therapeutists, the deep seated forms of tuberculosis of early life which, whether or not they may be benefited by treatment, almost never as a matter of fact receive such treatment—until too late. We do not as yet know how far the almost universal tuberculization of our race is accompanied by a tuberculous process in the lungs, as well as in the tracheobronchial lymph nodes, discoverable by physical diagnosis or otherwise. We do not even know whether immunization may not necessarily depend upon past or present tuberculous disease, whether the distinction between tuberculous infection and tuberculous disease after all may not exist.

Many familiar facts would seem to invite inquiry along such lines. We know of the practical universality of tuberculosis of the tracheobronchial nodes; we know that the small parenchymatous focus, the Ghon focus if you please, is very common. This focus with its enlarged regional hilum nodes and with the peribronchial and perivascular lymphangitis about the vessels which connect focus and nodes, presents a complete pulmonary tuberculosis in miniature. We know that localized thickenings of the lines which proceed to the lower lobes from the hilum are very frequently seen. Such thickenings are often ascribed to other causes. Their tuberculous nature is proved if, as is often the case, the thickened lines are accompanied by dots which can hardly be accounted for as anything else than tuberculous lymph nodes. When did this process run its course, this deep tuberculosis now soundly healed? What is its significance as to prognosis? How frequent is it?

When it was reported that some 86,000 French soldiers had fallen victims to tuberculosis under the conditions of military service, apprehension was felt by some in America lest our soldiers might also become a prey to the same disease. But at a later time it appeared that the large majority of these men had been rejected at entrance into the army, and therefore had not acquired their disability in the military service; also, that there was doubt whether the major portion of those in whom tuberculosis had been diagnosticated really had that disease. On the other hand, one authority thinks that these soldiers really had tuberculosis, but an abortive and healed tuberculosis which did not incapacitate for service. Such uncertainties as to the diagnosis of tuberculosis have led to error in all of the principal armies engaged in the late war. The example is cited as an illustration of the great practical importance to the world in war, as well as in peace, of greater clarity in our views as to the minor abnormalities of the upper lobes. When such abnormalities are found in otherwise healthy persons, are they to be ascribed chiefly to atelectasis and congestion, or to nontuberculous induration, or to a healed tuberculosis, or are many of the signs in reality not evidence of abnormalities at all, but due to the proximity of the bronchi?

We know that not only do the lower lobes in health show markings ascribable to tuberculosis, but that quite as frequently similar localized thickenings of the lines which ascend from the hilum to the upper lobes are apparent in the radiograph, with or without other evidences of tuberculosis in persons never known to have been ill. We do not know from a large series of observations whether there is such a constancy between the physical findings and those of the X-ray as to indicate that both series of phenomena are due to a single cause. Such questions are epidemiological questions, only to be solved by a long and unremunerative process of research which the physician cannot be expected to undertake unaided. They are at the same time relatively simple questions and easy of approach, sufficient time and money being given. They should be carried out, not upon patients who believe themselves ill or are ill, but upon a multitude of healthy individuals, fair representatives of the population at large.

From the standpoint of the epidemiologist, it is surprising how little interest has been excited by the remarkable fact of the existing widespread infection with tuberculosis and how few are the investigations which seek to get at the root of the matter.

For example, we hear constantly that tuberculin is of little value in adults, because so many of them react to it and very similar statements are made as to the complement binding reaction. But both the cutaneous and the complement binding tests are too insensitive to reveal all of the tuberculous infection. The important point—what is the meaning of the negative percentage in these reactions—seems never to be considered.

In the description of a disease, the natural method is to bring out most prominently its characteristics as they are found in the majority of the cases. Tuberculosis stands alone among the common and serious diseases which afflict mankind in that its characteristics, as they appear in the large majority of the infected population, receive but scant consideration and, indeed, have practically not been studied at all.

My point will be clearer if we put the matter as follows: The tubercle bacillus is a highly resistant and widely disseminated microörganism, which no person living in our present civilization can long escape. The result of the incorporation of the bacillus is sooner or later an inflammatory reaction, which in most cases passes unnoticed. The majority of the population does not develop a tuberculosis, which is clinically manifest, according, at least, to our present criteria, however great the exposure to the disease may subsequently be and however bad the hygienic conditions. A certain minority in the population, however an undesirably large minority, say one to seven or one to ten, fares less well. They develop a disease, usually of the lungs, which often proves fatal, though frequently ending in more or less complete recovery or arrest. Such cases may properly be called the failures in tuberculous infection.

From such a standpoint, it would appear that the conspicuous success of the majority in escaping the evil results of a grave infection of which they have been the subjects, might be worthy of serious consideration. We may well ask ourselves what it is that enables the majority to escape. How do they differ from the unfortunate minority who perish in the same surroundings? The answer must be we do not know. We know at least what is not the chief reason for the development of manifest tuberculosis. It is not bad air, nor bad food, nor bad hygiene, nor overwork, nor race, nor unhealthy climate, for the majority of the numbers of our civilization who are subjected to those various unfavorable influences escape. And if we take refuge in the word "predisposition," that is merely another name for ignorance. What percentage of civilized adults fail to react to the cutaneous tuberculin test with undiluted tuberculin? How many of those negative to the cutaneous test, after repeated applications, can be made to react to tuberculin administered intracutaneously or subcutaneously? If there remains a negative percentage after such tests, what is to be thought of the existence of tuberculous infection in such cases? In remote rural communities where manifest tuberculosis has long been absent, does a negative reaction to tuberculin mean absence of infection or a high resistance? What is the meaning of a negative reaction to tuberculin in cases of bone and joint tuberculosis, in persons apparently healthy, who are employees of tuberculosis sanatoria or are otherwise much exposed to infection, or in patients known to be tuberculous, yet at work and in fairly good health?

We need to know the conditions of the infection which results so favorably in the majority, as contrasted with the cases which terminate fatally. Is it a mere matter of dosage? Should the primary infection be minimal in amount, or does a large dose of tubercle bacilli determine a more vigorous reaction and give a better prognosis? In what year of life is it best that infection should first take place, or (what is not necessarily the same thing) become evident through reactivity to tuberculin?

Each independent pathologist seems to erect his own standards as to what is or is not to be considered evidence of a past tuberculosis; with the inevitable result of a considerable discordance in the findings of the individual investigators. This was conspicuous in the attempts made to determine the percentage of tuberculosis found at the autopsies of combatants in the late war. There can be no question that a not overwhelming tuberculous infection produces an allergy, call it immunity or not, as you please, which profoundly affects the reaction of the tissues for an indefinite period. Such changes of reaction should be more marked among the successes than among the failures in tuberculous infection and more marked in a ripened resistance than in a newly established process. How strange that this point has not long ago attracted universal attention! The fact is that we know much about the phenomena of a recent artificial infection, but almost nothing about the minute details of the pathological histology of the small and long-healed tuberculous lesion and as little of the slowly and intermittently progressive, comparatively benign deep tuberculous process in the lungs.

What disease so abounds in paradoxes as does tuberculosis! It is at once the most trivial and the most deadly of diseases. It has swept away whole tribes, living in perfect health in a salubrious climate, yet the teeming millions of the Orient continue to multiply despite its constant presence. The immortal discovery of Jenner robbed smallpox of its terrors, but at the expense of producing a local lesion not without its discomforts and even dangers. The "great white plague" on the other hand, the most universal and the most constantly dreaded of diseases, effects a vaccination against itself in the bodies of the majority of mankind so easily, so painlessly, that the child passes through the momentous transformation unnoticed.

We have sought in vain to force tuberculosis into the mould of other infectious diseases: it is a law unto itself. We have learned enough to see that it is a disease which must be studied without prepossessions, to see that its immunity though no less real is not like the immunity of other diseases, that it can only be comprehended by taking into consideration the facts of the disease as it manifests itself in every clime and in every social status. Above all, we must not fail to study with care the tuberculosis of the uncared for, unstudied majority of civilized mankind, for in the success unconsciously attained by this majority lies the hope of rescuing the minority who now fall beneath the scourge of tuberculosis. For the study of this tuberculosis of the majority we need the accumulation of data by epidemiological investigations, which should be prolonged beyond the usual period of activity of a single investigator, and which would require expenditures beyond the purse of the individual and of local institutions. If our attitude as physicians has been individualistic and our investigations parochial in scope we should not be blamed; we have done the best that we could as individuals, with the time, the clinical opportunities and the money at our disposal. For the broad view and for extended investigation is needed the guidance of a governing body, immortal in life because constantly renewed in membership, which can initiate a universally applicable policy; a body which shall garner and sift the results of observations extending over the world through the lifetime of more than one generation; a body which, because it is international, shall be bound to follow no master and shall not be tempted through patriotism to exalt the findings of the one, nor to depreciate the findings of the other school; which shall contain minds of the keenest logical powers to get at the very root of the matter, not forgetting *advocatus diaboli* to pick flaws if possible in such conclusions as may be reached;—a body, too, which by its eminence and its world-wide connections shall be able to loose the pursestrings of capital and command abundant resources. Where can such a body be found better than in the International Union Against Tuberculosis?

In my opinion this body has an unrivaled opportunity for research, aside from the eminence of its members, in that it may assume work that is too prolonged, too tedious and too expensive for the ordinary investigator.

I had prepared a list of subjects worthy of investigation, but the time is short and moreover it would be superfluous, even impertinent, to attempt suggestions to such an audience more competent than I to institute investigations of this kind. I cannot, however, resist the desire to impress upon you one thought. It is this: a basal fact in phthisiology which has been established beyond the shadow of a doubt is that the large majority of civilized mankind are infected with tuberculosis. That they do not die of it is the best of proofs that tuberculosis is not necessarily an evil. May it not indeed be that the salvation of the people is to be sought in an optimal tuberculization? The hope of entire freedom from infection with tuberculosis is surely illusory under present conditions.

We have learned by bitter experience that war can only be conducted successfully with the aid of a perfect coöperation and, wherever practicable, a thorough standardization. The existence of the International Union shows that our leaders are alive to the advantages of international coöperation in the study of tuberculosis. Under their leadership, may we not look forward to standardizing our knowledge, to compelling the assent of the world by the accumulation of mountains of proved objective facts, so that some of the problems of to-day shall become the truisms of to-morrow, so that there may be laid, broad and deep, everlasting foundations upon which our successors shall go on to build a perfect structure?

In the preceding remarks upon the subject of the relations of the International Union Against Tuberculosis to investigations of the difficult problems of tuberculosis, I have endeavored to maintain as objective an attitude as possible and to speak only of the simpler facts of tuberculosis in the simplest words. Yet it is impossible to avoid language which shall reveal the speaker's standpoint. You know perfectly well what my views are. Furthermore, it is safe to say that you do not agree with me. I am perfectly sure that the majority of my hearers do not share all of my views. Now it is always pleasant for a speaker to feel that he carries his audience with him. But if I could have believed that you would agree with me, this address would not have been made. For the point of it all is our differences—our differences as to the fundamental questions, the basal facts of phthisiology. If the members of a body like that which I have the honor to address were all in accord upon those questions, the world would be ready to build upon that solid foundation for which it has so long waited in vain. But you, on the one hand, and I upon the other, both parties with every desire to know the truth, see the truth in different ways: we are not in accord as to the fundamentals, perhaps do not agree as to what the fundamentals are. I have mentioned what I considered gaps in our knowledge, which it is desirable should be filled. My fundamentals are stated by way of examples as to lack of knowledge and lack of agreement. I have no wish to impose and no expectation of imposing my views upon you for your acceptance. I am not wedded to my views; all that I desire is the truth—that is all that you desire. But we differ; that is another very good example of lack of agreement.

Let us at least agree that the lack of agreement is regrettable. Let us do something to remove this stigma upon our science, I care not what, so long as the work accomplished brings as its reward some irrefutably established principles; some courses, however apparently insignificant, upon which in time the foundations may be completed, the superstructure begin to rise.

SMALL PNEUMOTHORAX IN TUBERCULOSIS

(Abstract of a monograph)

NATHAN BARLOW AND JAMES C. THOMPSON[1]

The limited space at our disposal makes it necessary to defer all explanations, discussions of abstruse questions, references to literature, and acknowledgements of indebtedness to our detailed report; and, as a consequence, only those applications of our work which are most obvious can be even mentioned in so brief a paper. In presenting a report of a condition which has important and practical applications to both the diagnosis and treatment of tuberculosis, but which has been almost entirely overlooked by the keenest investigators up to the present time, we feel that a brief explanation is due as to why the frequency of the condition has not been recognized before.

We owe the greater part of our knowledge of disease conditions and the interpretation of physical signs to the pathologist. We have very justly come to feel that any interpretation of physical signs or clinical symptoms, which cannot be confirmed at autopsy, must have conclusive proof of some other nature before it can be accepted. The small pneumothorax which we are considering is not a permanent pathological change of the pulmonary tissues, but it is a temporary displacement of tissue and usually disappears before or during the terminal illness. The few which do persist are destroyed when the pleural adhesions are separated at post mortem. As these temporary structures are very frequent in tuberculosis, and rarely, if ever, occur in other diseases, the changes in the physical signs which they produce have naturally been considered as due to the pathological changes which were evident at the autopsy.

A pneumothorax is easily recognized in X-ray plates only when it extends from the anterior to the posterior wall of the thorax, so that there is an area upon the plate which is entirely free from lung markings. The smaller ones which we are considering are very seldom situated in exactly that location, so that there is usually no area upon the plates which is free from pulmonary markings and, if the displacement is either anterior or posterior, there may not even be any definite area of decreased density. The diagnostic criterion is therefore a definite separation of pleural surfaces. This can only be perceived in stereoscopic plates taken by a technique adapted to its demonstration in that particular patient, so that while routine stereoroentgenograms will demonstrate this separation in a certain number of patients, in many cases it is necessary to give special attention to the details of technique which are discussed in our report. The actual vision of separation of the pleural surfaces requires not only facility in the use of the stereoscope, but also, in the majority of cases, considerable experience in the study of small pneumothorax. If the detection of a small pneumothorax depended entirely upon the attention being attracted by this separation, we doubt if we ourselves would find more than a small percentage of the small pneumothoraces which are present.

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Fortunately, the changes produced in the arrangement of the markings are of such a nature that they can be usually recognized as different from those which occur in pulmonary tuberculosis unaffected by pneumothorax. We have called these peculiar arrangements and distributions of densities "indicating signs." We describe a number of these in our report. The most easily recognized are deviation of the trachea and mediastinum, annular shadows, and bands and zones of density and rarefaction which do not conform to those which would be expected from any probable course of development of a tuberculous process. The deviation of the trachea or of one wall is the most easily perceived of any of these, is usually angular when recent and points toward the side on which the pneumothorax occurs. That is to say, that while in large pneumothoraces, the trachea, mediastinum, or heart are deviated toward the opposite side, in small localized pneumothoraces the deviation is toward the side on which the pneumothorax lies. Annular shadows lying either at the surface of the lung, or in the region of the interlobar septa, occur in a certain percentage of localized pneumothoraces in these regions and when present afford an easily recognized indicating sign. Areas of rarefaction and bands or zones of density which do not conform to the ordinary locations of a tuberculous process and which are difficult to explain are often produced by localized pneumothorax and when present should lead to scrutiny of the plates.

We classify small pneumothorax in different ways. The most obvious classification is into a superficial and deep group: the superficial comprising all those in contact with the pleura of the thoracic wall, and the deep group comprising all those which lie entirely upon the mediastinal or interlobar surfaces of the lung. Clinically, the most useful classification is into central and lateral groups. The central group includes all those which lie in relationship to the median half of the lung. The lateral group includes not only those of the superficial group which lie over the lateral half of the lung, but also interlobar pneumothoraces which are large enough to approach the lateral surface of the lung.

The formation of these small pneumothoraces is discussed in detail in our monograph. Briefly, it depends upon the fact that adhesions are first formed and are densest at the periphery of a tuberculous area. The mediastinal and central forms are likely to be long and tubular, because the heart, in front, and the great vessels, behind, tend to preserve by their pulsation two bands of pleural surface which remain free from adhesion. The frequency with which these small pneumothoraces are found depends largely upon the technique of both the X-ray and the physical examination and the amount of skill and experience in their detection. It seems that nearly every case of tuberculosis at some time or other presents one or more of these structures. In a careful study of over a thousand cases of nontuberculous disease, we have found no instances of the presence of a small pneumothorax in the areas which are characteristic of tuberculosis. The partial pneumothorax which occasionally occurs in streptococcic pneumonias and similar conditions is entirely different in size and location and should cause no confusion.

The striking physical signs which are characteristic of large partial or complete pneumothorax are not usually encountered in the small forms which we are considering. The metallic phenomena, marked tympany, and complete suppression of all breath sounds are not characteristic of very small pneumothorax. With one or two possible exceptions there is no single sign which cannot be produced by other pathological conditions. It is natural, therefore, that the changes in the signs which are caused by small pneumothorax should have been attributed to other and more generally recognized changes, and that many examiners have adopted a technique which accentuates the physical signs least affected by the presence of a localized pneumothorax, and have learned to disregard the discrepancies in the results of different diagnostic procedures, which we so constantly encounter in the course of our physical examinations.

The physical signs of the superficial group are more obvious than those of the deep group. On inspection, deviation of the trachea may be perceived, together with the usual signs of early tuberculosis. On palpation, deviation or broadening of and distortion of the trachea may be perceived. Changes in the muscles, and other palpation signs of early tuberculosis are usually found, and occasionally the pneumothorax may be outlined by palpation of the tactile fremitus.

The primary percussion change of a small pneumothorax is the production of true tympany as distinguished from hyperresonance. Owing to thickening of, or deposits upon, the pleura, this soon becomes dulness, with or without a tympanitic overnote and may simulate ordinary hyperresonance or impaired resonance. In the collapsed area, slight or marked dulness is of course to be expected. Percussion often indicates a localized pneumothorax, by revealing a deviation of the mediastinum toward the affected side. We have found that small cavities usually produce diminished dulness or slight resonance, rather than tympany. A cavity large enough to produce tympany usually gives a low pitched tone, while the tympany of small pneumothorax is usually high pitched. It is sometimes possible to outline both cavity and pneumothorax from the difference in the pitch and quality of the tympany heard over adjacent areas. It may be noted here that the cavities remaining after complete destruction of a considerable part of a lobe by an acute process have their lateral walls formed by pleura alone. The mechanical conditions are so similar to those produced by a corresponding pneumothorax that the diagnosis by physical examination or by X-ray is very difficult. The differential diagnosis is discussed in our monograph.

In early tuberculosis and in slowly progressing, moderately advanced tuberculosis, the majority of the conditions which are diagnosed as "superficial dry cavities" are not really cavities, but small pneumothoraces in which the physical signs are unusually striking. It should be remembered that a small pneumothorax often adjoins or is fused with a cavity of appreciable size, and the physical signs may be due in part to one and in part to the other. We have found that the Wintrich change usually (but not always) indicates a cavity which may or may not be overlain by a small pneumothorax. The cracked pot sound seems to be more often produced by a cavity and pneumothorax, or by two cavities which communicate, then by a single cavity alone. On auscultation, the changes in the whispered signs are those which are most particularly characteristic of small pneumothorax. Whispered pectriloquy, especially if of high pitch or with an amphoric quality, is much more characteristic of small pneumothorax than it is of cavity. Whispered pectoriloquy which has two different pitches at different points on the chest is usually due to a cavity which communicates with a small pneumothorax. An extension of the tracheal quality of whisper beyond normal limits is usually due to a pneumothorax of the central group. On the contrary, spoken pectoriloquy and bronchophony are usually well marked over cavities, but not over small pneumothoraces, unless there is free communication with a bronchus.

In the region adjoining a small pneumothorax, ringing or altered bronchophony or even egophony may be produced, whether fluid be present or not. The breath sounds are increased and often given an amphoric quality in recent pneumothoraces which communicate with or are in contact with a bronchus; if in contact with the trachea, the tracheal quality is accentuated. An entirely superficial pneumothorax causes diminished breath sounds, and the formation of pleural exudate causes a diminution of the intensity of all auscultatory phenomena in course of time. Friction sounds cannot of course be produced in a pneumothorax but, over the surrounding adhesions, slight friction sounds of various sorts are frequently heard.

Equally striking are the changes in physical signs produced by the collapse of the lung tissue in the immediate neighborhood of the pneumothorax. These on a small scale are similar to those produced by a complete pneumothorax. The most striking changes are those produced in the râles. If the active process is confined entirely to the region affected by the pneumothorax, the râles may be entirely suppressed. Otherwise they are reduced in number and constancy and their quality is altered. They usually give less of an impression of moisture, and the time of their appearance in the respiratory cycle varies irregularly. We have found a consonating quality added to the râles more frequently by pneumothorax than by a cavity. We usually allude to the altered râles heard in the neighborhood of localized pneumothorax as *partly suppressed râles* or *collapse râles*. They include some, but by no means all, of the râles which are variously described as dry, sticky, viscid, atypical, abortive, peculiar, etc. The changes in physical signs in this collapsed area are those usually associated with consolidated tissue. The breathing is more or less bronchial and may be diminished. The voice sounds are increased as a rule, and are often altered in quality: they may be ringing, may have an amphoric quality, and in some cases a true egophony may be heard. Posttussive puff and posttussive suction frequently occur over pneumothorax communicating with a cavity.

The diagnosis by physical signs must therefore depend upon an interpretation of arrangements and groupings of physical signs which cannot otherwise be fully explained. These are discussed in detail in our larger report. The diagnosis of mediastinal and interlobar small pneumothorax is frequently possible by physical signs, but the discussion would be too long to be given here, as it involves certain distinctions which are usually disregarded, and assigns an entirely new significance to at least one of the well known physical signs (d'Espine's sign).

The symptoms of onset are often so slight that the patient does not notice them. When present, they are similar to those of large pneumothorax; sudden sharp pains in the chest, slight sudden dyspnea, sometimes blood spitting, or occasionally a hemhorrage, nausea, faintness, palpitation, etc. The clinical symptoms resulting from its presence include pain in the chest, particularly substernal pains, disturbances of blood pressure and pulse rate when the region of the great vessels or pericardium is affected by the process, slight dyspnea, and the whole train of reflex symptoms which follow irritations of the pleura. These include dilatation of the pupil, trophic disturbances as of muscles, radiating pains, alterations of the voice and, if the diaphragmatic pleura be involved, reflex disturbances of the abdominal walls and viscera.

The immediate effect of a localized pneumothorax depends entirely upon the proportion of the diseased tissue which is collapsed after the formation of the pneumothorax. In very early tuberculosis, it is much more likely that the entire involved region may be more or less collapsed by the pneumothorax. In such cases there may be a complete suppression of râles, and the effective reduction of the absorption of poisonous products from the tuberculous focus may be such that the clinical symptoms of the disease almost entirely disappear, and as a result the patient will show neither the physical signs nor the clinical symptoms of tuberculosis. Such a patient is in a condition somewhat similar to one under treatment by artificial pneumothorax. The case may seem to be apparently arrested, when in reality the lesion is not healed, but is merely collapsed. This collapse of the tissue favors the development of fibrosis and if the patient remains under treatment will very considerably hasten his cure; but if both the patient and the physician are deceived by the absence of physical signs and clinical symptoms, and the patient returns prematurely to the stresses and strains of ordinary life, there will be great danger of reactivation and relapse.

In advanced tuberculosis, the amount of tissue collapsed is likely to be so small a part of that involved in the active process that it makes but little difference in the general condition of the patient. In such cases the occurrence of the pneumothorax is likely to be signalized by chill and fever followed by several days of elevated temperature, and then a brief period of apparent improvement. In some of these cases, the pneumothorax is intermittent, alternately closing and opening.

The problem of diagnosis is not to determine whether there is a localized pneumothorax or not; if the patient has tuberculosis, it is most probable that the pleural surfaces enclose one or more small air pockets. The problem is to determine whether the collapse permitted by the air pockets which are present is sufficient in amount and of such location with reference to the tuberculous infiltration that it can materially modify the physical signs and clinical symptoms and course, and consequently the method of handling the case.

In the beginning of the study, both the clinician and the roentgenologist will recognize only the more obvious pneumothoraces, and neither one can advance rapidly in their study if unaided. With such mutual aid, the constant agreement of physical signs and X-ray appearances leads to finer and finer diagnosis, until after several months both the clinician and the roentgenologist will easily detect the greater number of those which are present.

In two years' work with several thousand patients we have found that these small pneumothoraces occur only in tuberculosis. But tuberculosis in this sense is by no means always manifest tuberculosis. Tuberculosis at the hilum, or near the interlobar septa, if at all active, usually reaches the pleura at some point, whereupon it almost invariably produces a deepseated localized pneumothorax. The presence of a localized pneumothorax, therefore, indicates an active tuberculous process, which may be anything from an active central infection, such as is ordinarily referred to as "latent tuberculosis," "hilum tuberculosis," a "pretuberculous stage," etc., up to and including far advanced and terminal phthisis. In general, then, a patient should not be told that he has tuberculosis (meaning manifest tuberculous disease) merely because a localized pneumothorax is detected upon physical examination or upon the X-ray plate. On the other hand, if a localized pneumothorax is found, the examiner may be entirely certain that there is an active tuberculous process present, that if the patient has had a manifest phthisis, he is still in danger of relapse, and that if the disease has not as yet reached the manifest stage, the patient's life should be so ordered as to prevent the development of consumption. We by no means imply that every case of tuberculous infection which shows a deep-seated small pneumothorax will develop a manifest tuberculosis unless he is placed under treatment, but we have found no case either in children or adults which presented a small pneumothorax and which did not at the same time show unmistakable signs of illness and constitutional impairment, often slight and of limited duration.

While no doubt many, probably the majority, of such cases will recover without treatment, the percentage which ultimately develop a progressive pulmonary tuberculosis will certainly be considerably larger among such cases than among those which present only the entirely inactive and nonprogressive infection which is evident only at autopsy.

We have carefully studied those of our patients who have been discharged from this or other hospitals as quiescent or apparently arrested, or who have felt so well that they have refused to remain longer under treatment, and who at later periods have returned to us with reactivation or relapse. We find that of these patients 82 per cent have had localized pneumothoraces of such situation and extent that they cause partial or complete collapse of all parts of the lung showing any considerable tuberculous infiltration. It seems likely, therefore, that a thorough understanding of the effects of small pneumothorax will enable us to determine certain of the cases which are liable to relapse and which need to remain longer under treatment or observation.

While patients are still under treatment those who have a partially effective collapse from localized pneumothorax will show less moisture and fewer clinical symptoms than will patients with the same amount of involvement but not receiving the benefits of small pneumothoraces which are favorably situated with reference to the lesions. This group of patients can easily be separated by physical examination and by the study of the X-ray plate, and should receive a somewhat more rigid treatment than would seem to be indicated by the examination and by the clinical chart.

The size and position of the small pneumothoraces which may be present sometimes have an important bearing upon both the selection of cases for treatment by artificial pneumothorax and the administration of the general and special treatment.

The practical importance of a thorough understanding of the diagnosis and effect of small pneumothorax is therefore sufficient to justify the months of attention and study which must be given toward it by the clinician and roentgenologist in collaboration, before proficiency and certainty in diagnosis can be obtained. Numerous special applications of importance are given in our monograph. The more obvious and general ones are as follows:

1. The explanation of the absence of signs of moisture in cases which otherwise seem to have an active tuberculous lesion.
2. An explanation which enables the physician to understand certain of the vagaries in the course of tuberculosis which are otherwise inexplicable.
3. The determination of a certain number of the cases which need more careful supervision than the same amount of clinical activity would ordinarily indicate.
4. The determination in advance of a certain proportion of the quiescent and apparently arrested cases which are particularly liable to relapse.
5. Assistance in the selection and in the treatment of certain of the cases which may be considered for treatment by artificial pneumothorax.
6. The division of the cases usually diagnosed neurasthenia, debility, autointoxication, etc.; in other words, cases of ill defined general illness into two classes, in one of which a tuberculous infection of slight extent or central location plays some part, and in the other of which there is probably no active tuberculous element whatever.

THE EFFECT OF ARTIFICIAL PNEUMOTHORAX ON THE COLLATERAL LUNG

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Artificial pneumothorax has attained a high place as a therapeutic procedure in pulmonary tuberculosis, and has gradually but consistently gained in general favor since its inception about four decades ago. First used by only a few, and in hopeless and advanced cases, the procedure is now more widely employed in selected cases in all stages of the disease. The advent of the roentgen ray and its application to chest diagnosis, and in the administration of artificial pneumothorax have helped to elucidate many otherwise vague findings and results. In former days it was an axiom that pneumothorax should not be performed unless the collateral lung was uninvolved. Practical experience, however, soon showed the fallacy of this idea and the impossibility of finding the clear cut unilateral case. It is difficult to estimate the number of cases of pulmonary tuberculosis in which collapse therapy has materially harmed or made the disease progress on the treated side: the percentage varies with the individual experience, but the general consensus of opinion is that most cases are benefited. It is even more difficult to determine the percentage of cases in which the collateral uncollapsed lung has been detrimentally affected by the treatment.

Schill (1), in an excellent recent communication, has aptly divided the opinions of the various observers on the latter phase of this subject and classifies them into three groups. So far as he was able to observe, however, no direct studies on this subject had been made. In the first group was included those observers who believed that the pneumothorax exerted a harmful effect upon the collateral lung: the actual cases however, included only a small percentage of the cases treated (12 to 15 per cent). In the second group was included those who believed that the pneumothorax exerted a beneficial effect upon the collateral lung; the cases reported in this group were also not numerous. In the third group was included those who believed that the pneumothorax had very little effect, if any, upon the collateral lung: this was by far the more prevalent opinion. In concluding, Schill notes that in those cases, which were definitely reported as harmed on the collateral side, the period of observation was extremely short; and that the cases were of the acute pneumonic and malignant types, considered unsuitable for any treatment, and therefore worthless in so far as they indicated any accurate estimate of the treatment. In suitable cases, and where the observations were extended, artificial pneumothorax could exert a beneficial effect upon the collateral lung. He strongly recommends a prolonged period of observation before drawing conclusions.

In a purely anatomical study of the human chest in health and disease, Nitsch (2) describes two thin and flexible spots in the mediastinum which are especially prone to transmit an effect on the collateral lung, following artificial pneumothorax. The one lies anteriorly, directly behind the sternum, at the site of the atrophied thymus gland, and is variable in size. The other lies posteriorly in the vicinity of the large vessels, bounded by the spinal column and aorta behind, and the esophagus and heart anteriorly.

In order to determine the value of accurate manometric readings in artificial pneumothorax, Muralt (3) elaborately studied the effects of various conditions in the treated side of the chest upon the manometer. He found that, although pressure readings were susceptible to a great many individual influences, on the whole the findings were fairly constant and could be profitably analyzed as regards the position of the needle, the condition of the pleural space, the condition of the mediastinum, the amount of gas resorbed and that necessary to maintain compression, the early diagnosis of an exudate, and the presence of a perforation of the lung or a valvular pneumothorax. He pointed out that it is necessary to make all comparative manometric readings in the same relative position, since there is a distinct difference in pressure in the different interspaces, both anteriorly and posteriorly. The observations to be reported in this paper concern mainly a clinical and roentgenological study of a number of cases of pulmonary tuberculosis, in which special attention was paid to the effect of artificial pneumothorax on the collateral lung. In order to gain an insight into the effect of artificial pneumothorax upon the collateral lung from a physiological standpoint, manometric readings of both pleural cavities were made in man and goats.

THE EFFECT OF PNEUMOTHORAX UPON THE MANOMETRIC READING IN THE COLLATERAL PLEURAL SPACE

In order to determine the difference between the manometric readings at different intercostal levels a normal goat was used and intrapleural manometer readings were made on both sides of the chest consecutively. During the entire period of experiment the goat was kept under a uniform, medium ether anesthesia. Readings were made at the first, third and fifth interspaces on both sides, about midway between the sternum and spinal column before and after the introduction of air into the right pleural cavity. The results of the manometric readings are given in table 1.

TABLE 1

*Bilateral pleural manometric readings in goat before and after right sided artificial pneumothorax**

AMOUNT OF AIR INJECTED INTO THE RIGHT PLEURAL CAVITY	PLEURAL CAVITY	WATER MANOMETER READINGS IN CENTIMETRES IN INTERSPACE					
		First		Third		Fifth	
Before	Right	+0.0	−1.5	+0.0	−4.0	+0.0	−3.0
	Left	+0.0	−1.5	−1.0	−4.0	+0.0	−3.0
After 50 cc. on right side	Right	+4.0	−2.0	+0.5	−1.5	+4.0	−3.0
	Left	+2.0	−2.5	+3.0	−3.0	+4.0	−2.0
10 minutes after an additional 50 cc.	Right	+4.5	−2.0	+4.0	−1.0	+4.0	−3.0
	Left	+4.0	−3.0	+5.0	−3.0	+5.0	−3.0

* This experiment was duplicated in another goat with about the same general results.

An analysis of these readings, allowing for some irregularities in the breathing of the animal and other uncontrollable factors connected with experiments of this character on animals, indicates that the intrapleural manometric readings on the collateral side closely parallel those on the treated side before and after the production of artificial pneumothorax.

Our study of the intrapleural pressure in man was limited to three cases, two that had previously had an artificial pneumothorax and one that was initially treated. The technique employed was identical to that used in the goat, care being taken to make all readings as nearly comparable as possible and to introduce the needle at about the same level and in the same interspace on both sides. The readings were made with a water manometer which was connected to the two needles through a two-way cock, so that the pressures on the two sides could be read consecutively and within a short time of each other. The needles used were also of large calibre (16 gauge in man and 14 gauge in the goat) and the same for both sides to allow easy access to the manometer. Three cases were studied with the results given in table 2.

TABLE 2

The effect of artificial pneumothorax upon the collateral lung as indicated by the intrapleural pressure

CASE	SIDE OF PNEUMOTHORAX	TOTAL AMOUNT OF AIR INTRODUCED BEFORE READING WAS MADE	WATER MANOMETER READING IN CENTIMETRES				NOTES ON THE CASES
			Right pleural space*		Left pleural space		
		cc.					
1	Right (had 12 previous fillings begun 3 months before)	000	+0.0	−3.0	+0.5	−2.0	Male, 35 years. Pulmonary symptoms began 1½ years ago with spitting of blood. General condition good, slightly overweight. Physical examination reveals involvement of the right apex. Right pneumothorax begun 3 months before study. Sputum negative. Ambulant case.
		100	+0.0	−2.0	+0.5	−0.0	
		300	+0.5	−2.0	+0.5	−0.0	
		500	+0.5	−1.5	+0.5	−0.5	
		600	+1.0	−1.5	+0.5	−0.5	
		650	+1.0	−1.5	+0.5	−0.5	
2	Left (had 15 previous fillings begun 3½ months before)	000	+0.0	−1.0	+1.5	−0.5	Male 34 years. Hospital case. Cavity in upper left lobe, active advanced case, tubercle bacilli positive. Ambulant case at time of test. Left pneumothorax begun 5 months before study.
		100	+0.5	−0.5	+2.0	+0.5	
		150	+1.0	−0.5	+2.0	+0.0	
		200	+1.0	−0.5	+2.5	+0.5	
3	Left (initial filling)	00	−1.0	−3.0	−1.0	−3.0	Female, 24 years. Sanatorium case. Slight involvement of both apices with peribronchial thickening. Tubercle bacilli negative. Initial left pneumothorax begun with this study.
		50	−0.0	−2.0	−0.0	−2.5	
		100	−0.0	−2.0	+0.5	−1.5	
		200	−0.0	−2.0	+1.0	−1.5	
		250	+0.5	−1.0	+1.0	−1.0	

* During the making of manometer readings postural changes were carefully avoided, since it was found that these would materially affect the readings.

An examination of this table reveals that an artificial pneumothorax on one side of the chest affects the intrapleural pressure on the opposite side and this effect is probably transmitted to the corresponding (collateral) lung.

THE EFFECT OF PNEUMOTHORAX UPON TUBERCULOSIS IN THE RABBIT'S LUNG AFTER THE INTRAVENOUS INJECTION OF TUBERCLE BACILLI

In previous investigations reported from the Research Department of the National Jewish Hospital for Consumptives (4), it had been found that one-sided artificial pneumothorax or compression of one of the lungs of the rabbit by means of fluid, artificial hydrothorax, has no visible macroscopic influence upon the number or type of the tuberculous lesions resulting from the intravenous injection of virulent human tubercle bacilli, regardless of whether the compression was occasioned on the right or left side, or whether it was occasioned a day before or a day after the intravenous injection of the tubercle bacilli. No difference was noted between the number or type of the tuberculous lesions in animals with one lung compressed as compared with normal animals, not compressed, although the difference between the different animals of the same series receiving the same intravenous injections of tubercle bacilli was greater than the differences found between the two lungs of the same animal. Prolonged artificial pneumothorax (5) in rabbits, sufficient to induce a good collapse of the right lung, initiated shortly after the intravenous injection of a suspension of virulent human tubercle bacilli, and maintained for a period of a month by means of the intrapleural injection of air every second or third day throughout the experimental period, also had no appreciable effect upon the size or number of macroscopic tubercles found in the lungs of the treated animals as compared to the untreated, or in the compressed right lung as compared to the uncollapsed left lung. These experiments were conclusive as far as they went; but it seemed desirable to study the effect of the pneumothorax upon a more advanced tuberculosis in elaboration of the above studies. For this purpose a series of 12 mature and healthy rabbits was given intravenous injection of a uniform suspension of virulent human tubercle bacilli, and after one month when the tuberculosis had well developed an artificial pneumothorax was instituted on the right side and maintained by intrapleural air injections at two or three day intervals for another three weeks, after which there remained 4 control rabbits untreated and 3 pneumothorax rabbits. Briefly stated, the results obtained did not differ from those obtained in the experiments previously reported. Prolonged artificial pneumothorax in rabbits, sufficient to induce a good collapse of the right lung, initiated one month after the intravenous injection of a suspension of virulent human tubercle bacilli and maintained for a period of three weeks by means of the intrapleural injection of air every second or third day, had no appreciable effect upon the size or number of macroscopic tubercles found in the lungs of the treated animals as compared to the untreated, or in the compressed right lung as compared to the uncollapsed left lung.

THE EFFECT OF ARTIFICIAL PNEUMOTHORAX UPON THE CHEST ROENTGEN RAY FINDINGS

The animal experiments cited above would indicate that in so far as the macroscopic tuberculosis of the lungs is concerned, artificial pneumothorax treatment exerted no appreciable influence upon the disease in the two lungs, at least within a short period of time. In spite of this, X-ray chest pictures taken in men treated with artificial pneumothorax would indicate early and rapid changes occurring in the collateral lung. Unfortunately X-ray chest studies in animals are beset with many difficulties, so that this source is not available for a solution of this problem. It was for this reason that a series of chest plates of patients was carefully studied in the hope of elucidating the apparent inconsistency between these results. The cases, of which seven are presented, are given in three classes and in the following order: two in which the roentgenograph shows no appreciable or only a slight change; three in which the roentgenograph reveals apparent definitely increased pathological changes; and two in which the roentgenograph reveals apparent definitely diminished pathological changes in the collateral lung. A brief clinical record of the seven cases follows:

Case 1. No appreciable change in the roentgenographs of the collateral lung, taken before and six days after a partial artificial pneumothorax on the left side. Female, age forty-five years, housewife, entered the National Jewish Hospital for Consumptives with slight fever, night sweats, hemoptysis, chills and loss of weight. Upon admission, examination of the left lung revealed numerous moist râles throughout, after expiratory cough. Resonance was impaired, a friction rub was heard and vocal fremitus was increased. Dry râles were found at the apex of the right lung, with increased vocal fremitus and the rest of this lung was normal. Artificial pneumothorax was performed on the left side, November 4, 1920; and six days later, after two administrations of gas, a roentgenograph was taken which revealed partial compression of the left lung; but, in comparing the roentgenograph of the right lung before and six days after establishing the left artificial pneumothorax, there does not seem to be any appreciable difference between the density of the mottling at the end of this time. (See figures 1 and 2.)

Case 2. A slight increase in tissue density in the roentgenograph taken three months after a good left sided artificial pneumothorax in comparison to that found in the collateral or right lung before pneumothorax. Male, age thirty-four years, cigar dealer, entered the hospital, July 13, 1920, with fever, hemoptysis, weakness, cough, expectoration, pain in the chest and night sweats. Physical examination revealed impaired resonance over both lungs with moist râles after expiratory cough, vocal fremitus increased over both apices and bronchial breathing. The upper left lobe contained a cavity. The sputum contained tubercle bacilli. Artificial pneumothorax was performed on the left side, November 4, 1920, and maintained until discharge, May 7, 1921, when the patient was recorded as greatly improved. In comparing the roentgenographs taken before and three months after the initiation of artificial pneumothorax, the right or collateral lung seems to reveal a slight increase in density at the end of this time while the collapse attained was good. (See figures 3 and 4.)

Case 3. A definite increase in the tissue changes in the roentgenograph taken five months after a good left sided artificial pneumothorax in comparison to that found in the right (collateral) lung before pneumothorax. A male, age thirty-seven years, a clerk, admitted to the National Jewish Hospital for Consumptives, February 15, 1919, with cough, expectoration, fever and night sweats. Physical examination revealed extensive involvement of both lungs, with bronchovesicular breathing, impaired resonance and râles over the entire chest wall anteriorly and posteriorly. A large cavity was found in the left infraclavicular region. The sputum contained tubercle bacilli. Artificial pneumothorax was performed on the left side August 26, 1919, and on January 9, 1920, fluid was noticed on this side, which persisted for several months and then disappeared. The patient was discharged June 14, 1920, improved. A comparison of the roentgenographs, taken before and five months after the initiation of artificial pneumothorax, revealed the right or collateral lung to be definitely more involved (increased tissue density) at the end of this time. The collapse attained was good. (See figures 5 and 6.)

Case 4. A definite increase in the tissue density in the roentgenograph of the left (or collateral) lung taken nine days after a marked right sided artificial pneumothorax as compared to that found before this treatment. A male, age thirty years, a clerk, was admitted to the hospital, May 15, 1918, with cough of two years duration, night sweats, fever, dyspnoea on exertion, and hemoptysis. Physical examination revealed involvement of the right lung anteriorly above the first rib and posteriorly from the sixth dorsal spine up, with moist râles and bronchovesicular breathing. The sputum contained tubercle bacilli. The X-ray report indicated far advanced pulmonary tuberculosis of the right lung, adhesions to the right diaphragm, the heart displaced to the right, and multiple cavity formation on the right side with scattered consolidated areas. In the left lung there was fibrosis in the lower lobe and areas of scattered consolidation. Artificial pneumothorax was performed on the right side, December 2, 1918. The patient was discharged greatly improved November 6, 1919. A comparison of the roentgenographs taken before and nine days after the initiation of artificial pneumothorax revealed the left or collateral lung to be definitely more involved (increase in tissue densities) at the end of this time. The collapse attained was marked for the time interval. (See figures 7 and 8.)

Case 5. A definite increase in the lung density in the roentgenograph of the right collateral lung, taken one month after a good left sided artificial pneumothorax as compared to that found before this treatment. A male, age nineteen years, a drug clerk, entered the hospital with hemoptysis, fever and cough on November 20, 1917. Physical examination revealed impaired resonance and bronchial breathing over the left apex, and numerous fine râles over the left apex and from the fourth rib up anteriorly and the third dorsal spine up posteriorly on the left side. There was impaired resonance over the right apex, with bronchovesicular breathing and a few râles. Tubercle bacilli were found in the sputum. The X-ray report indicated a diffuse mottled involvement of both lungs. Artificial pneumothorax was performed on the left side, January 29, 1918. A comparison of the roentgenograph taken before and one month after the initiation of artificial pneumothorax revealed the right or collateral lung to be definitely more involved (increase in lung density) at the end of this time. The collapse attained was good. (See figures 9 and 10).

Case 6. A diminution in the lung density in the roentgenograph of the right collateral lung, taken nine months after a good left sided artificial pneumothorax as compared to that found before treatment. A male, age twenty-seven years, a clerk, was readmitted to the hospital October 25, 1919. At this time there was dulness over both apices, and the resonance was impaired anteriorly, bilaterally from the third rib up. A few dry râles were heard at the right apex and all over the entire left side anteriorly and posteriorly. The breath sounds were bronchovesicular over the right apex, bronchial over the left apex, and bronchovesicular over the entire left side. Fluoroscopy revealed a small cavity in the left upper lobe at the level of the first interspace. The sputum contained tubercle bacilli. Artificial pneumothorax was performed on the left side February 19, 1920, when a good collapse was attained. The patient was discharged very much improved and able to work, March 30, 1921. A comparison of the roentgenographs taken before and nine months after the initiation of artificial pneumothorax revealed the right or collateral lung to be less involved (decrease in lung density) at the end of this time. The collapse at this time was fair. (See figures 11 and 12.)

Case 7. A definite diminution in the lung findings in the roentgenograph of the right collateral lung, eleven months after a marked left sided artificial pneumothorax as compared to that found before treatment. A male, age thirty-two years, a tailor, entered the hospital, December 31, 1918, with cough and hemoptysis. Physical examination revealed impaired resonance over the entire left lung, vocal fremitus being increased in the left upper lobe, and moist râles were heard after expiratory cough over the entire left lung. In the right lung there were a few scattered râles, with some impairment of resonance in the upper lobe. The sputum contained tubercle bacilli. Artificial pneumothorax was perfomed on the left side May 26, 1919. The patient was discharged May 26, 1921, improved. A comparison of the roentgenographs, taken before and eleven months after the initiation of artificial pneumothorax, revealed the right or collateral lung to be definitely less involved (a decrease in the lung density) at the end of this time. The collapse at this time was good, there also being fluid in the left pleural cavity. (See figures 13 and 14.)

TABLE 3

Summary and classification of the clinical cases of artificial pneumothorax according to the X-ray findings in the collateral lung

CASE	INTERVAL BETWEEN THE INITIAL ARTIFICIAL PNEUMOTHORAX AND THE LAST ROENTGENOGRAPH	GRADE OF COLLAPSE ATTAINED	EFFECT OF ARTIFICIAL PNEUMOTHORAX UPON THE ROENTGENOGRAPH OF THE COLLATERAL LUNG
1	6 days	+*	Not appreciable
2	3 months	++	Slightly increased lung density
3	5 months	++	Definitely increased lung density
4	9 days	+++	Definitely increased lung density
5	1 month	++	Definitely increased lung density
6	9 months	++	Diminished lung density
7	11 months	+++	Definitely diminished lung density

* The grade of collapse obtained is graded arbitrarily, but approximately from — = no collapse to +++, a complete and maximum clinical collapse of the treated lung.

Although there are certain apparent difficulties in comparing different roentgenographs even from the same individual, it seems that this study has brought out a number of definite points which can best be seen by tabulating the above cases as is done in table 3.

SUMMARY

A study of the tabulation of the seven cases of artificial pneumothorax in man reported above seems to bring out several important points:

1. That the pulmonary roentgenographic findings in the collateral lung after artificial pneumothorax in cases of pulmonary tuberculosis may be definitely increased and in so short a time, within nine days, after this treatment, that they would not appear to be due to actual pathological changes.

2. That these increased roentgenographic findings in the collateral lung, occurring shortly after the initiation of artificial pneumothorax, are probably due to the intensification of the already existing pathological changes.

3. That the preliminary roentgenographic changes seen in the collateral lung are in some way dependent upon the pressure from the treated side exerted against the mediastinum.

4. That after prolonged treatment with artificial pneumothorax a diminution of roentgengraphic findings may occur in the collateral lung which would indicate a decreased pathological change in the lungs of these cases.

5. That bilateral tuberculous involvement alone does not necessarily contraindicate the use of artificial pneumothorax.

I wish to acknowledge my appreciation of the material assistance received from Drs. H. J. Corper, O. B. Rensch and H. Gauss during the preparation of this paper.

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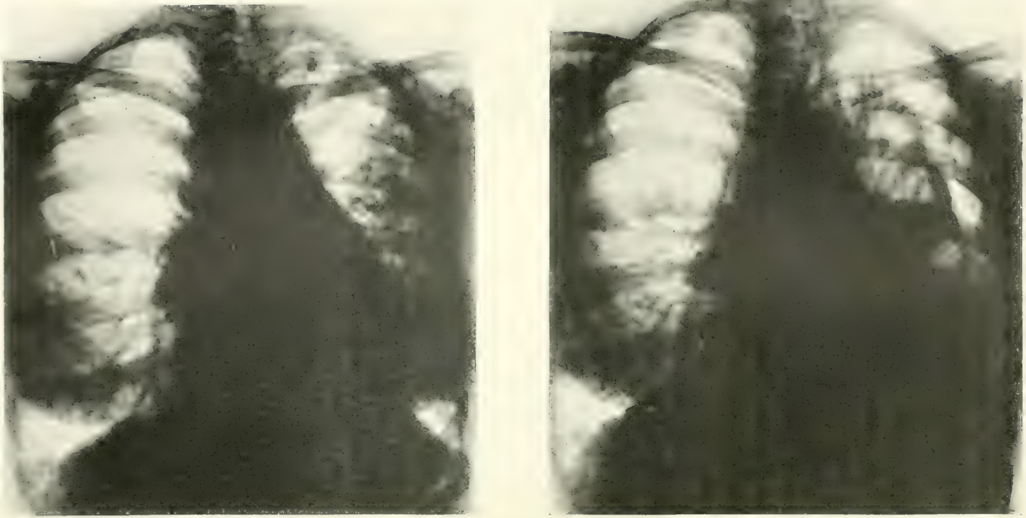

FIG. 1. BEFORE ARTIFICIAL PNEUMOTHORAX

FIG. 2. SIX DAYS AFTER ARTIFICIAL PNEUMOTHORAX

FIG. 1 AND 2. Case 1. Roentgenographs show no appreciable change in the right lung six days after incomplete compression of the left.

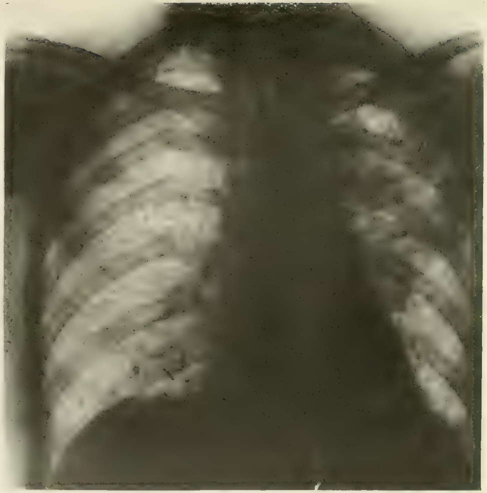

FIG. 3. BEFORE ARTIFICIAL PNEUMOTHORAX

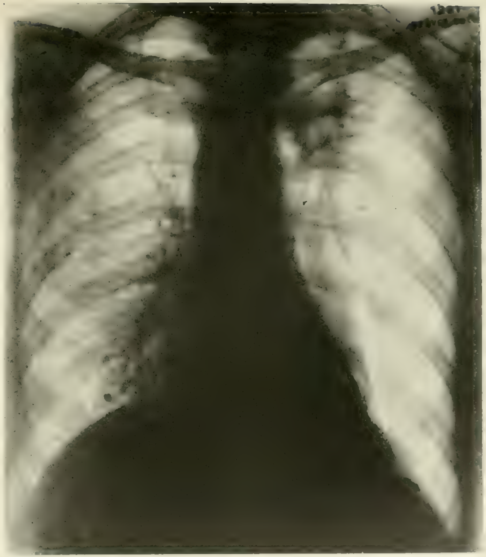

FIG. 4. THREE MONTHS AFTER INDUCTION OF PNEUMOTHORAX

FIG. 3 AND 4. Case 2. Roentgenographs show a slight increase in the findings in the right lung three months after a fairly complete left-sided compression.

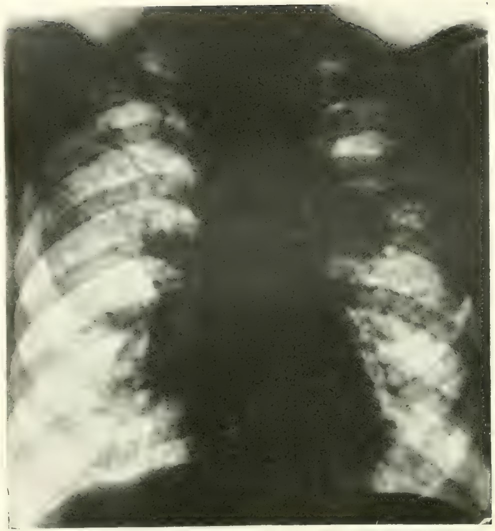

Fig. 5. Before Artificial Pneumothorax

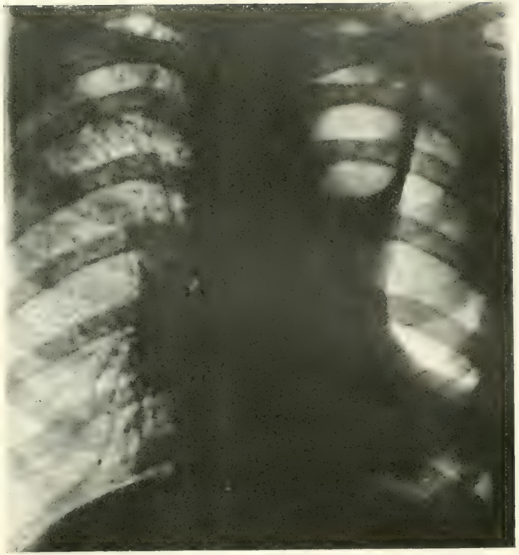

Fig. 6. Five Months after Induction of Pneumothorax

Fig. 5 and 6. Case 3. Roentgenographs show a definite increase in the findings in the right lung five months after a fairly complete left-sided compression.

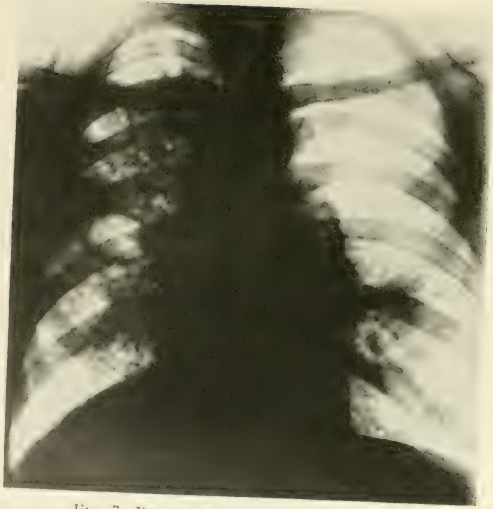

Fig. 7. Before Artificial Pneumothorax

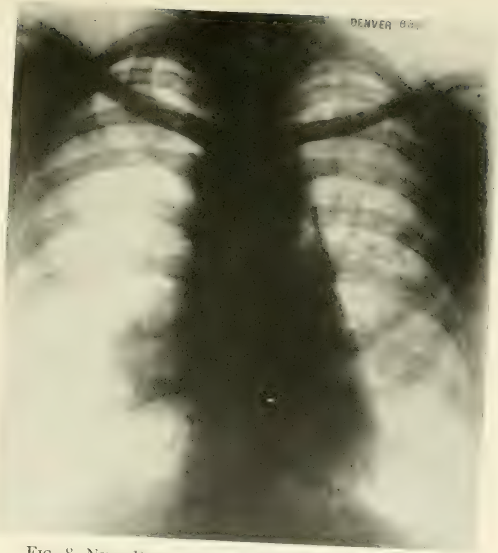

Fig. 8. Nine Days after Artificial Pneumothorax

Fig. 7 and 8. Case 4. Roentgenographs show a definite increase in the findings in the left lung nine days after complete compression of right.

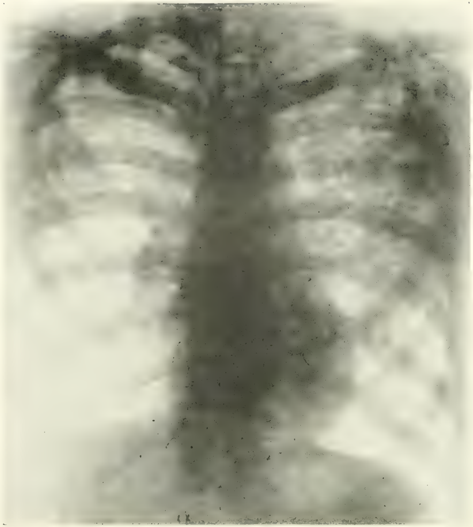

FIG. 9. BEFORE ARTIFICIAL PNEUMOTHORAX

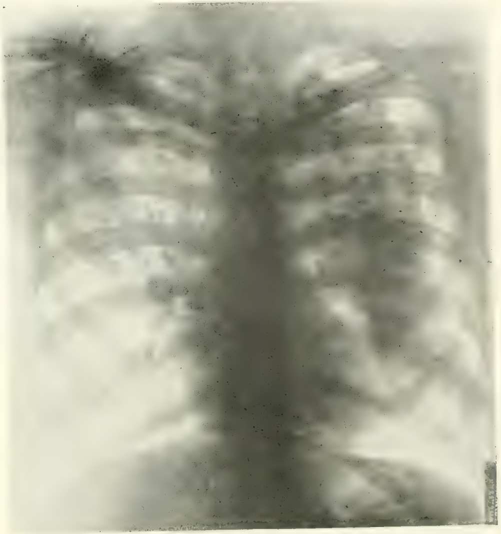

FIG. 10. ONE MONTH AFTER INDUCTION OF PNEUMOTHORAX

FIG. 9 and 10. Case 5. Roentgenographs show a definite increase in the findings in the right lung one month after a fairly complete left-sided compression.

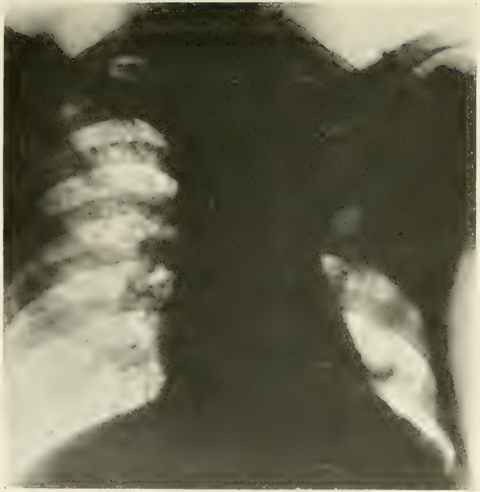

Fig. 11. Before Artificial Pneumothorax

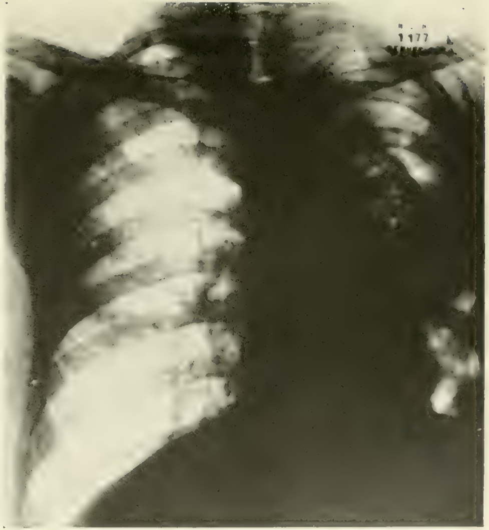

Fig. 12. Nine Months after Induction of Pneumothorax

Fig. 11 and 12. Case 6. Roentgenographs show a diminution in the findings in the right lung nine months after a fairly successful left-sided compression.

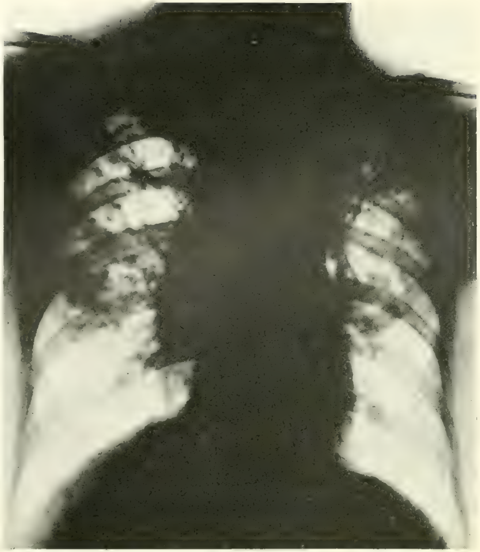

FIG. 13. BEFORE ARTIFICIAL PNEUMOTHORAX

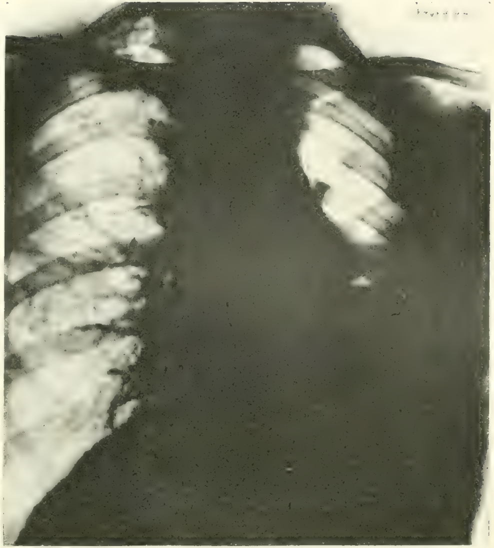

FIG. 14. ELEVEN MONTHS AFTER INDUCTION OF PNEUMOTHORAX

FIG. 13 AND 14. Case 7. Roentgenographs show a definite diminution in the findings in the right lung eleven months after a complete left-sided compression.

THE EFFECT OF NITROUS OXIDE, NATURAL GAS AND FORMALDEHYDE ON EXPERIMENTAL TUBERCULOSIS

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The primary purpose of this investigation to determine the effect of repeated nitrous oxide anesthesia on tuberculous guinea pigs proceeded from the hope that some information might be gained which would aid in the search for a suitable anesthetic for tuberculous patients requiring surgical anesthesia. In connection with this, I made an attempt to demonstrate, if possible, the deleterious influence of constant irritation of the respiratory passages with formaldehyde or of the general lowering of the vitality of infected animals by repeated applications of natural gas.

Tuberculosis, as naturally found in man, is in many respects different from the artificially produced tuberculosis of the guinea pig. In the former, we usually find a prolonged course with constant attempts toward fibrosis and healing, remission of symptoms and activity, and relapses of varying intensity, which are greatly influenced by external factors, such as exercise, living conditions, pregnancy, intercurrent disease, nutrition and other environmental agents. In the guinea pig experimental infections usually pursue a progressive course, uninfluenced by external factors and, because of this fact, exact comparisons cannot be drawn. However, the guinea pig is usually chosen for experimental investigations on account of its availability and its susceptibility to tuberculous infection.

From the general observations of many clinicians (1) we well know the detrimental influence of ether anesthesia on patients with pulmonary tuberculosis, while the investigations of Corper (2) Brown and Petroff (3) and Rogers (4) indicate that the lesions of tuberculous animals are uninfluenced by ether anesthesia. Doubtless the explanation of the different effects of ether in the two conditions is that in man the irritating properties of ether on the respiratory mucous membrane cause, first, labored respiration and, second, an increase of the secretions, thus diluting the germ laden sputum and facilitating an aspiration of the infectious material into unaffected areas of the lung, where it may produce new foci of infection. In the guinea pig, lung tubercle is more of the pneumonic or solitary form and positive sputum is apparently absent.

In an effort to determine the influence of the aforesaid gases on tuberculous animals, the following experiments were conducted: Guinea pigs were wrapped in thick cloths, in such way as to leave only the anterior nares exposed, and then placed in a box suitably prepared to protect the operator from the infectious particles. The animals were then sprayed with a no. 15 De Vilbiss atomizer which contained a suspension of fresh, bacilli-positive, tuberculous sputum in water. After keeping the animals in the atmosphere of finely divided sputum for a period of one to three minutes, they were unwrapped and given a 1 to 5000 bichloride of mercury bath. In a previous communication it has been shown that animals can be infected in this way with marked regularity (5), tubercles becoming visible in the lungs on the seventh or ninth day, while in the liver and spleen they appear on the eighteenth. Objections naturally arise in regard to this method of infection, since the dose cannot be accurately gauged, and it is also difficult to devise a scheme by which the operator can be entirely protected. By this method, however, the earliest and most marked lesions are produced in the lungs, and the inhaled material will come in direct contact with the developing tubercles: also, by the use of sputum, the other microörganisms which might influence the pathological changes are present.

Experiment 1. July 29, 1920: 26 adult guinea pigs were infected by spraying and divided into two groups of 13 each. Twenty-four hours after spraying, those in group 1 were put in a closed box with a glass top, through which the animals could be observed and given nitrous oxide through a connecting tube until anesthesia was obtained. When respiration became embarrassed, oxygen was given in sufficient quantity to restore normal respiration. They were kept under complete anesthesia for fifteen minutes each day for nine successive days without any fatal results due to the gas: 3, however, died from epidemic pneumonia. The rest were killed and sectioned on August 29, 1920. The experiment resulted as follows:

Anesthetized group

ANIMAL	EMACIATION	LUNGS	LIVER	SPLEEN	LYMPH NODES
1	Moderate	++++	++++	Negative	++++
2	Moderate	++++	++++	++	++
3	Moderate	++	++++	Negative	+++
4	Moderate	++++	++++	++++	++++
5	Moderate	+++	++	Negative	++++
6	Marked	++++	++	Negative	++++
7	Moderate	++++	++	Negative	+++
8	Moderate	+++	++++	++++	++
9	Moderate	++	++++	++++	+++
10	Moderate	++++	++++	+	++

Note: The lesions were scored from + to ++++, + denoting minimum and ++++ maximum involvement.

The animals in group 2 were used as controls and not anesthetized after infection. Five of them died from pneumonia before the disease developed, and of the remaining 8, 4 died later and were examined. The results in these 4 were as follows:

ANIMAL	DATE OF DEATH	FINDINGS
1	August 12, 1920	Generalized tuberculosis
2	August 16, 1920	Generalized tuberculosis
3	August 28, 1920	Generalized tuberculosis
4	August 29, 1920	Generalized tuberculosis

The remaining 4 were killed at the same time as those in the anesthetized group and showed the following lesions:

ANIMAL	EMACIATION	LUNGS	LIVER	SPLEEN	LYMPH NODES
1	Moderate	++++	+++	++	+++
2	Moderate	+++	++++	++++	++
3	Moderate	++++	+++	+++	++++
4	Moderate	++	++	++++	++

Experiment 2. August 17, 1920: Ten, adult male guinea pigs were infected as in *experiment 1.* They were then divided into two groups, one consisting of seven animals for anesthesia and the other of three for controls. On September 1, 1920 the nitrous oxide anesthesia was begun and repeated daily until September 16, when all animals in both groups were killed and examined. The results follow:

Nitrous oxide treated animals

ANIMAL	EMACIATION	LUNGS	LIVER	SPLEEN	LYMPH NODES
1	Moderate	++++	++++	++++	−
2	Moderate	++++	++++	++++	+
3	Marked	++++	++	+++	+
4	Moderate	++++	++	+++	−
5	Marked	++++	++++	++++	−
6	Moderate	++++	++++	++	−
7	Moderate	++++	++++	++++	−

Control animals

ANIMAL	EMACIATION	LUNGS	LIVER	SPLEEN	LYMPH NODES
1	Moderate	++++	++++	++	+
2	Moderate	++++	+++	++	+
3	Moderate	+++	++++	++++	+

From the results of *experiment 1*, one might be led to the casual conclusion that the repeated inhalations of nitrous oxide and oxygen had favorably influenced the general health of the treated animals, since 10 of the anesthetized group survived at the end of thirty days, while only 4 of the controls remained. However, the fact must not be overlooked that the extent of the tuberculous involvement in an animal must be used as the criterion instead of the duration of life (Krause (6), Corper (7); therefore, the results shown in the first and second tables demonstrate no distinct difference between the amount of tuberculosis in animals anesthetized with nitrous oxide twenty-four hours after infection and continuing for nine successive days and that in the control animals. Likewise, after allowing the disease to develop for fourteen days without interference, and then administering repeated nitrous oxide anesthesia, no influence was to be noted, as shown in *experiment 2*.

Experiment 3. To test the influence of natural gas and formaldehyde on developing tubercle, the following experiments were conducted: On August 17,1920, eleven guinea pigs were infected by spraying as in *experiment 1*, the animals having previously been divided into three groups. Group 1 consisted of 4 pigs which, immediately after spraying, were placed in a closed box equipped with a glass top through which the animals could be observed, and were then given enough natural gas through a connecting tube to produce asphyxiation. The gas was then turned off, the box opened, and the animals allowed to revive. This process was repeated daily for seventeen days. After this, the animals were caged and not subjected to gas for a period of twenty-three days, at the end of which time they were killed and the lesions noted as follows:

ANIMAL	LUNGS	LIVER	SPLEEN	LYMPH NODES
1	++++	+++	+++	+++
2	++++	–	+++	++++
3	+++	++++	++++	+++
4	++++	++++	++++	+++

Group 2 consisted of 3 guinea pigs. These were placed in a closed box containing a piece of cotton saturated with formaldehyde, and allowed to remain in the fumes until one of the group was overcome. They were then removed and given opportunity to revive in the fresh air. The first inhalation was given twenty-three hours before infection and thereafter every day for fifteen days. They were killed and examined forty days after infection, with the following results:

ANIMAL	LUNGS	LIVER	SPLEEN	LYMPH NODES
1	++++	+++	++	++++
2	++++	++++	++++	++++
3	+++	+++	+++	+++

Group 3 consisted of 4 guinea pigs which, after infection, were turned outside on the hospital grounds surrounding the laboratory. There they fed on the grass and were left unmolested until forty days after infection, when they were killed and autopsied along with groups 1 and 2, and showed the following lesions:

ANIMAL	LUNGS	LIVER	SPLEEN	LYMPH NODES
1	++++	++++	+++	+++
2	+++	+++	+	+++
3	+++	++++	+++	++++
4	+++	+++	+++	++++

After carefully recording the lesions found in these three groups at necropsy and tabulating them from + to ++++, thus indicating the minimum to maximum involvement, respectively, no distinct difference could be noted between the animals that receive daily inhalations of natural gas after infection for seventeen days and the control group; neither was there any marked variation to be observed in the groups that received daily inhalations of formaldehyde fumes, beginning twenty-four hours before infection and continuing daily for fifteen days thereafter.

CONCLUSION

Neither repeated nitrous oxide and oxygen anesthesia, nor formaldehyde nor natural gas influence the development or progress of the tubercle in guinea pigs infected through the respiratory route with a watery solution of tubercle bacilli positive sputum.

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STUDIES WITH MORPHINE IN EXPERIMENTAL TUBERCULOSIS

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The modern treatment of tuberculosis, based upon rest, food and fresh air, remains the essential rational therapeusis since Bodington in 1840 emphasized these major points. However, some important adjuvants have been added, such as artificial pneumothorax, the orthopedic immobilization procedures and operative measures (for instance, Albee's bone graft treatment of Pott's disease), the postural treatment of pulmonary tuberculosis advocated by Webb and his colleagues, the recent chest belt advocated by Sewall and the sedative drugs, all measures to produce localized rest and thus limit the disease. So too could be added the important, though often neglected, nutritional discoveries, like the value of antiscorbutics and vitamines and the proper use of sun and artificial light treatment. The abuse of any of these or their misuse by unintelligent hands may in all cases be disastrous. One would be radical to condemn these procedures because they have failed in the hands of the untrained who are unable to recognize the contraindications to their use.

Opium and its derivatives is one of the most condemned drugs; however, in proper hands it is one of the most valuable therapeutic agents that we have. Its alkaloids have been advocated on numerous occasions for use in pulmonary tuberculosis. As early as 1891 Dill (1) recommended the smoking of opium mixed with tobacco in pulmonary tuberculosis; not as a cure for consumption, but as palliative and an aid to treatment; not as a substitute for the treatment which professional skill and experience have been led to adopt, but as a possible aid to it. Van Marter's (2) experience with the modified opium smoking advocated by Dill led him to conclude "that it seldom harms and often does much good." Solomon Smith (3) stated, "It may be taken as a broad rule that in the treatment of phthisical cough, sedatives should not be mixed with cough mixtures to be taken frequently, but that when required they should be given in sufficient doses, not merely to mitigate, but for the time to cure cough, and so give a period of rest, and that before giving them all proper measures should be taken to remove reflex causes of irritation." Sakorrafos (4) believes as a result of his experience in using morphine on patients that this drug is a valuable medicament in tuberculosis. Gaussel (5) obtained good results with pantopon, a mixture of 50 per cent morphine and 40 per cent of the other alkaloids of opium, in tuberculosis.

Appreciating the sedative action of opium, acknowledging the importance of rest in tuberculosis, and cognizant of the beneficial results reported by clinicians from the use of sedatives in pulmonary tuberculosis, we undertook to study the effects of morphine upon experimental tuberculosis, to determine whether we could observe any improvement in the experimentally produced tuberculosis following its administration. Its direct action upon the tubercle bacillus was also observed.

THE EFFECT OF MORPHINE UPON TUBERCLE BACILLI IN CULTURES

The studies to be reported in this paper are entirely experimental, and concern the effect of morphine on the tubercle bacillus, the effect of the tubercle bacillus on morphine, and morphine's effect upon experimental tuberculosis in the guinea pig. Morphine, even in saturated solution, is not tuberculocidal for short intervals up to three days. To determine whether, however, morphine in soluble salt form as sulphate has an inhibitory influence upon the growth of tubercle bacilli the following experiments were performed:

To a series of bacteriological test tubes containing 10 cc. of sterile 5 per cent glycerol agar was added varying amounts of pure sterile morphine sulphate (Powers and Weightman), from 0.06 to 65 mgm. After mixing the constituents well, the glycerol agar containing the morphine was slanted and inoculated with cultures of human tubercle bacilli, an avirulent culture "Old Human" and a virulent culture "Pasternack." These tubes were then incubated at 37.5° C. and examined after intervals of one, two, three and four months incubation and the growth recorded with the results given in table 1.

An examination of table 1 reveals that morphine sulphate, in amounts as small as 1 mgm., incorporated in 10 cc. of glycerol agar, completely inhibits the growth of human tubercle bacilli during the first month of incubation; while during the second month growth occurs in the 4 mgm. concentration and during the third month and thereafter in the 16 mgm.

TABLE 1.

The growth of human tubercle bacilli upon glycerol agar containing morphine sulphate

AMOUNTS OF MORPHINE SULPHATE IN 10 CC. OF GLYCEROL AGAR	CULTURE OF TUBERCLE BACILLI	NUMBER OF TUBES INOCULATED	READINGS AFTER			
			One month	Two months	Three months	Four months
mgm.						
65.0	"Old human"	3	—	—	—	—
	"Pasternack"	5	—	—	—	—
32.5	"Old human"	3	—	—	—	—
	"Pasternack"	5	—	—	—	—
16.2	"Old human"	3	—	—	+	+
	"Pasternack"	5	—	—	+	+
8.1	"Old human"	3	—	—	++	++
	"Pasternack"	5	—	—	++	+++
4.0	"Old human"	3	—	—	+++	+++
	"Pasternack"	5	—	+	++++	++++
2.0	"Old human"	3	—	++	++++	++++
	"Pasternack"	5	—	+++	++++	++++
1.0	"Old human"	3	—	+++	++++	++++
	"Pasternack"	5	—	++++	++++	++++
0.5	"Old human"	3	+	++++	++++	++++
	"Pasternack"	5	+	++++	++++	++++
0.25	"Old human"	3	+	++++	++++	++++
	"Pasternack"	5	+	++++	++++	++++
0.12	"Old human"	3	++	++++	++++	++++
	"Pasternack"	5	++	++++	++++	++++
0.06	"Old human"	3	++	++++	++++	++++
	"Pasternack"	5	+	++++	++++	++++
None	"Old human"	3	++	++++	++++	++++
	"Pasternack"	5	++	++++	++++	++++

concentration. Above 16 mgm. of morphine sulphate there seems to be a definitely complete inhibition of growth. The explanation of this step-like gradation of growth during the different months either savors of the tolerance to morphine noted in mammals, or else it would seem that the tubercle bacillus is capable of actually destroying this activity of morphine and its salts. In order to roughly determine whether morphine was still present chemically in the culture medium at the termination of the experiment after four months, approximate quantitative analyses for morphine were made of the contents of a number of the tubes. Within the accuracy of the quantitative method used in the experiments at the time, the major part of the morphine seemed still to be present in the medium. Approximately from 80 in the larger amounts (down to the 16 mgm. concentration) to 60 per cent in the smaller amounts (down to the 2 mgm. concentration) was recovered.

In order, however, to study this point in greater detail a quantitative colorimetric method was developed which has been reported elsewhere (6), giving a quantitative accuracy from 0.10 to 50.0 mgm. of morphine sulphate in colloidal mixtures and tissues and an extinction point approximately down to 0.003 mgm. Using this method for the analyses and repeating the experiment given in table 1, but using in addition to the human tubercle bacilli a culture of bovine tubercle bacilli the results given in table 2 were obtained.

A careful examination of the findings depicted in table 2 reveals again a step-like gradation of the growth of both the human and bovine tubercle bacilli upon the glycerol agar containing the morphine sulphate in amounts varying from 65 mgm. in 10 cc. of agar to as low as 0.12 mgm. The analysis of the agar containing the morphine sulphate for this alkaloid at the end of ten weeks reveals an almost quantitative recovery of the morphine, so that the evidence obtained in this experiment would not seem to indicate that the tolerance could be explained on the basis of a destruction of the morphine by the tubercle bacillus.

In view of the fact that certain mammalian tissues *in vitro* were found in other studies capable of destroying the chemical entity of morphine to such an extent at least that its recovery by the ordinary methods of analyses was not possible, whether this change was due to oxidation or disintegrative changes was not determined (as indicated for beef liver in table 3) and made it seem highly desirable to determine whether tubercle bacilli *in vitro* could also destroy the chemical entity of morphine sulphate.

TABLE 2

The effect of the growth of tubercle bacilli on the morphine content of the medium upon which they have grown

AMOUNT OF MORPHINE SULPHATE IN 10 CC. OF GLYCEROL AGAR	CULTURE OF TUBERCLE BACILLI*	READINGS AFTER					RESULTS OF ANALYSIS FOR MORPHINE SULPHATE AFTER 10 WEEKS
		Two weeks	Four weeks	Six weeks	Eight weeks	Ten weeks	
mgm.							*mgm.*
65.0	"Pasternack"	—	—	—	—	—	62.7
	"Bovine"	—	—	—	—	—	61.6
32.0	"Pasternack"	—	—	—	—	—	31.5
	"Bovine"	—	—	—	—	—	27.2
16.0	"Pasternack"	—	—	—	—	—	15.5
	"Bovine"	—	—	—	—	+	15.3
8.0	"Pasternack"	—	—	—	+	+	7.6
	"Bovine"	—	—	—	+	++	7.8
4.0	"Pasternack"	—	—	+	+	+	3.5
	"Bovine"	—	—	+	++	++	3.7
2.0	"Pasternack"	—	—	+	+	++	1.37
	"Bovine"	—	+	++	++	+++	1.17
1.0	"Pasternack"	—	+	+	++	++	0.56
	"Bovine"	—	+	+++	+++	+++	0.53
0.5	"Pasternack"	—	+	++	++	+++	trace
	"Bovine"	—	++	+++	++++	++++	trace
0.25	"Pasternack"	—	+	++	++	++	0.0
	"Bovine"	—	++	+++	++++	++++	0.0
0.12	"Pasternack"	+	+	++	++	++	0.0
	"Bovine"	+	++	+++	+++	++++	0.0
None	"Pasternack"	—	+	++	+++	+++	0.0
	"Bovine"	+	++	++++	++++	++++	0.0

* Three tubes of each culture were inoculated and analyzed.

THE EFFECT OF BEEF LIVER AND TUBERCLE BACILLI UPON MORPHINE SULPHATE IN VITRO

The effect of beef liver upon morphine sulphate. Into each of eighteen small sterile flasks were placed 5 gm. of ground fresh beef liver and to this was added 5 cc. of sterile water. Nine of these flasks were heated for at least thirty minutes in a boiling water bath; and when cool, a solution of morphine sulphate containing 5 mgm. and 1 cc. of toluol was then added to all the flasks. After shaking well, one of the flasks containing the heated tissue and one containing the unheated tissue were analyzed to determine the amount of morphine sulphate remaining unchanged after intervals of from one minute to seventy-two hours' incubation at 37°C. with the results given in table 3. The flasks were frequently shaken and sufficient toluol kept in them.

TABLE 3

The effect of beef liver in vitro upon morphine sulphate

TIME INTERVAL OF INCUBATION UNDER TOLUOL AS ANTISEPTIC	MORPHINE SULPHATE RECOVERED IN MILLIGRAMS FROM THE	
	Heated tissues	Fresh tissues
One minute	4.86	4.83
Ten minutes	4.95	4.00
Twenty minutes	4.64	3.77
Thirty minutes	4.82	3.39
One hour	4.74	2.84
Two hours	4.54	2.77
Five hours	4.60	2.71
Sixteen hours	4.63	2.63
Seventy-two hours	4.91	2.36

It is noted from this experiment with beef liver that this tissue *in vitro* is capable of changing morphine sulphate chemically to such an extent that it cannot be recovered quantitatively by the method used.

The effect of tubercle bacilli upon morphine sulphate in vitro. In view of the fact that beef liver tissue is capable of destroying the chemical integrity of morphine sulphate, as seen from the above experiment, it seemed desirable to determine whether tubercle bacilli possess this same power. For this purpose 50 gm. of human and bovine tubercle bacilli (strains Miller (human), Knight (human), 4015 (human), Pasternack (human), a bovine avirulent and a bovine virulent) were removed with all aseptic precautions from the surface of the glycerol agar medium and placed in a sterile flask containing 40 cc. of sterile 0.9 per cent NaCl solution. After mixing well and breaking up all the lumps, the equivalent of 5 gm. of the tubercle bacilli was placed into each of ten small sterile flasks. Four of these flasks were heated in a boiling water bath for thirty minutes to destroy the enzymes present in the tubercle bacilli and, after cooling to room temperature, 5 mgm. of morphine sulphate in sterile solution and 1 cc. of sterile toluol were added to the ten flasks containing the heated and unheated bacilli. The cotton stoppered flasks were then carefully capped with heavy tin foil to prevent loss by evaporation and were incubated at 37°C., with frequent agitation and maintaining the presence of toluol for the entire period of incubation up to fourteen days.

TABLE 4

The effect of tubercle bacilli in vitro upon morphine sulphate

TIME INTERVAL OF INCUBATION UNDER TOLUENE AS ANTISEPTIC	MORPHINE SULPHATE RECOVERED IN MILLIGRAMS FROM THE	
	Heated tubercle bacilli mixture	Living bacilli mixture
One minute	4.80	4.78
One hour	—	3.43
One day	4.88	2.77
Four days	—	2.93
Seven days	4.65	2.86
Fourteen days	4.73	2.63

At certain intervals the flasks were removed from the incubator and ten volumes of 3 per cent trichloracetic acid solution added, shaken and the mixture heated in a boiling water bath for thirty minutes. Upon cooling, the contents of the flask were filtered, the precipitate washed at least five times with distilled water and the entire filtrate analyzed for morphine by the method previously described. The results of this study are given in table 4.

An examination of table 4 reveals that, like beef liver, tubercle bacilli possess the power of destroying the chemical entity of morphine sulphate; at least they alter this compound to such an extent that it cannot be recovered by the method of analysis used in these studies. To all intents and purposes this action seems to be enzymatic in nature, since it is destroyed by heating the bacilli in a boiling water bath for thirty minutes.

THE EFFECT OF MORPHINE UPON TUBERCULOSIS IN THE GUINEA PIG

Since morphine and its associated alkaloids probably have many properties, either beneficial or detrimental, still remaining to be discovered by the physiologist, and in view of their admitted hypnotic and sedative action, it seemed well worth while to determine what effect, if any, morphine would have upon experimental tuberculosis. So far as the available literature would indicate, no such studies had ever been made. Before, however, entering upon the therapeutic experiments it seemed well worth considering whether morphine as such could be considered as a direct therapeutic agent (7). In a series of experiments in which morphine sulphate was administered subcutaneously to guinea pigs, in amounts as large as 60 to 100 mgm. daily for a period as long as six weeks, and certain organs (the liver, lungs, spleen, brain, muscle and kidneys and tuberculous lymph nodes) analyzed for the presence of morphine, there was found to be no accumulation of morphine in any of these organs or in the tuberculous nodes; and within twenty-four hours after the last injection these tissues were entirely free from morphine in chemical form capable of demonstration. In view of this fact and the previously given cultural data it would seem highly improbable that this compound could have any direct therapeutic action in tuberculosis.

Since, however, there are no doubt other factors instrumental in retarding or hastening the progress of this disease in man and animals, and, since morphine seems to possess properties which could be considered advantageous under certain conditions, a study of the indirect effect of morphine upon experimental tuberculosis seemed desirable.

For this purpose a series of guinea pigs of uniform weight, and all males, were infected by injecting subcutaneously into the left groin small amounts (0.000,01 to 0.000,000,001 mgm.) (8) of virulent human tubercle bacilli. Some of these animals received no treatment and some of them received daily subcutaneous injections of morphine sulphate (8 mgm.), beginning one week before infection and continued to the termination of the experiment. In others the morphine injections were begun coincident with infection, and in another set the morphine injections were begun one week after infection. These animals were examined for the amount of tuberculous involvement in from five to seven weeks after infection with the results given in table 6. This experiment was suggested as a result of a preliminary experiment in which two different cultures of human tubercle bacilli ("Pasternack" and "Maxfield") were used for infecting and the period of study after infection was only of short duration. In this experiment there seemed to be a slight retarding influence of the morphine treatment upon the tuberculosis in the guinea pig. These results are given in table 5.

An examination of tables 5 and 6 reveals that small amounts of morphine sulphate (8 mgm.), given to guinea pigs daily before and during the early part of the infection (twenty-four days and five weeks), have a slight inhibitory effect upon the development of tuberculosis in these animals, while a prolonged period of treatment exceeding five weeks may not have an appreciable effect.

TABLE 5

The effect of small daily doses of morphine sulphate, given subcutaneously, upon tuberculosis in the guinea pig

TREATMENT*	CULTURES AND INFECTING DOSE USED			
	Pasternack		Maxfield	
	0.000,1 mgm.	0.000.000,1 mgm.	0.000,1 mgm.	0.000,000,1 mgm.
Controls (no treatment).............	+++†	+++	++	++
	+++	+++	++	Died
	++++	+++	++	Died
Eight milligrams morphine sulphate daily begun five days before infection and continued....................	++	++	++	+
	++	++	++	+
	+++	Died	+	+
Eight milligrams morphine sulphate daily given coincident with infection and continued....................	+++	++	++	+
	+++	++	++	+
	++	+	Died	+

* All the guinea pigs were sectioned twenty-four days after infection.

† The markings in this table conform with those previously reported from this laboratory and are as follows:

+ distinctly enlarged local (left inguinal) and slightly enlarged iliac lymph nodes.

++ enlarged inguinal and iliac nodes and slight involvement of the spleen.

+++ enlarged inguinal and iliac nodes, spleen markedly involved, tracheobronchial nodes enlarged and the lungs slightly involved.

++++ massive involvement of all important lymph nodes in path of infection, spleen, lungs and liver.

— no visible macroscopic tuberculosis.

In view of these slight but rather encouraging results in the animal experiments it seemed worth repeating these studies, and also to note the effect of the administration of larger doses of morphine sulphate given intermittently, that is, 130 mgm. given daily for three days, and then a three days' rest period followed by three days' treatment throughout the entire four weeks of infection. Daily injections of this amount of morphine sulphate for several weeks was found in preliminary experiment to be inconsistent with the life of the guinea pig. This was done and the results are incorporated in table 7, which also includes a study extending up to seven weeks after infection (series 2).

TABLE 6

The effect of daily injections of small doses (8 mgm.) of morphine sulphate upon tuberculosis in the guinea pig

AMOUNT OF TUBERCLE BACILLI (CULTURE MAXFIELD) INJECTED	INTERVAL BETWEEN INFECTION AND SECTION IN WEEKS	TREATMENT WAS BEGUN WITH RELATION TO INFECTION			
		Controls not treated	One week before	Coincident	One week after
mgm.					
0.000,01	Five	++* +++ ++	+ ++ + +	++ + + +	
0.000,000,1	Six	+ + +	+ + ++ +	+ (±) +	++ ++
0.000,000,001	Seven	+ + +	++ + +	++ ++ + ++	+ ++

* The gradings of tuberculous involvement are from — to ++++ as given in footnote to table 5.

An examination of table 7 reveals that the slight inhibitory effect of the morphine sulphate upon tuberculosis in the guinea pig, which is seen best in the early part of the infection up to four weeks, to a great extent disappears if the period of treatment and observation is extended to seven weeks.

In an attempt to seek the explanation for this slight inhibitory effect of the morphine sulphate upon tuberculosis in the guinea pig during the early stages, a number of possibilities suggested themselves. One of these was that it may be a purely chemical action, such as is seen in the effect of morphine upon the alkali reserve of the blood. Hjort and

TABLE 7

The effect of large doses of morphine sulphate, injected into guinea pigs, upon the development of tuberculosis

SERIES AND CULTURE	AMOUNT OF BACILLI USED FOR INFECTING	CONTROLS	TUBERCULOUS INVOLVEMENT		
			Subcutaneous injection of morphine sulphate		
			Large dose		Small daily doses (8 mgm.) daily throughout infection
			130 mgm. daily for 3 days followed by a 3 day rest and repeated throughout infection		
	mgm.				
Series 1. Four weeks infection period with culture "Maxfield"	0.001	+++* +++ +++	++ ++ ++		+ ++ +++
	0.000,1	++ ++ ++	+ + +		++ +
	0.000,01	++ ++ ++	+ +		+ + +
			Intermittent 3 days (130 mgm.)	Continuous daily (65 mgm.)	
	mgm.				
Series 2. Seven weeks infection period with culture "Levinson"	0.001	++++ +++ ++++ +++ ++++ +++	++++ +++ ++	++++ ++++ ++++	++ +++ ++++ ++ +++ +++
	0.000,01	++ +++ ++ +++ ++ +++	+++† +	+++ ++ ++ ++	++ +++ ++ ++++ ++ ++
	0.000,000,1	+++ +++ + +++ +++ ++	+++ +++ +++	+++ ++ +++ ++	+++ +++ +++ +++ +++

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* The grading of tuberculous involvement from — to ++++ is the same as in tables 5 and 6.

† With the larger doses of morphine sulphate a number of the guinea pigs in the series died before the termination of the experiment and are not recorded.

Taylor (9) found that morphine sulphate, administered subcutaneously to normal dogs, in doses of 10 mgm., caused an increase in the alkali reserve which is maintained at a high level for some hours, while our experiments (10) indicated that morphine administered subcutaneously in the form of sulphate to rabbits, dogs and sheep distinctly increased the alkali reserve of the blood plasma of these animals. Likewise there was a slight but distinct effect upon the pH of the blood plasma. Excitement in dogs and rabbits decreased the alkali reserve of the blood plasma. Repeated short interval injections of morphine did not tend to have a greater effect than a single injection. In man given a therapeutic or slightly toxic dose, morphine did not have a marked effect when administered subcutaneously (in dose from 16 to 32 mgm.) upon the pH or the alkali reserve of the plasma.

SUMMARY

Clinicians have reported beneficial results from the use of sedatives in tuberculosis. There are repeated instances in the history of medicine where drugs first employed empirically have later been shown to have a direct action in the disease for which they have been employed, and in some instances have even proved a specific—quinine is one of the best examples. Opium and its derivatives have much in their favor to recommend them therapeutically in tuberculosis. Their pronounced sedative action is entirely consistent with the great principle of rest in the rational therapeusis of this disease; nevertheless, it is quite true that other properties of these drugs may form equally strong contraindications for their use.

This study is concerned with the action of morphine on the tubercle bacillus and upon experimental tuberculosis in the guinea pig. Morphine, even in saturated solution, is not tuberculocidal for short intervals up to three days, whereas it does exercise a distinct inhibitory action upon the growth of the bacilli. The results indicate that morphine sulphate, in amounts as small as 1 mgm. incorporated in 10 cc. of glycerol agar, completely inhibits the growth of human tubercle bacilli during the first month of incubation (morphine diluted to 1 part in 10,000); and that during the second month growth occurs in the four milligram concentration, whereas after three months it occurs in sixteen milligram concentration. Above 16 mgm. (morphine diluted to 1 part in 625) there appears to be complete inhibition of growth. The ability of tubercle bacilli to grow in increasing concentrations with increased time is interesting and suggests the possibility of a morphine tolerance or morphine destruction. The morphine was recovered from the culture tubes practically quantitatively; whereas when morphine was mixed with a suspension of tubercle bacilli it was destroyed to a much greater degree, quite similar to the destructive action exercised by fresh liver tissue. When a quantity of morphine sulphate is mixed with emulsions of tubercle bacilli or liver cells, about half is so altered chemically that it can no longer be identified after twenty-four hours' incubation. Appreciably longer periods of incubation do not increase the amounts destroyed. There is much in this to suggest a ferment action. Further experiments are being conducted on this phase of the problem.

In experimental tuberculosis in the guinea pig, small amounts of morphine sulphate (8 mgm.), administered daily before and during the early part of the infection, have a slight inhibitory effect upon the development of the tuberculosis in these animals, while prolonged treatment exceeding five weeks after infection has little or no effect.

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THE VALUE OF FLAVINE COMPOUNDS IN EXPERIMENTAL TUBERCULOSIS

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Considerable attention has been devoted during the war, and since, to the use of flavine compounds and other basic benzol derivatives, especially in the treatment of infected wounds, acute urethritis and other diseases, where a germicide of high potency with no injury to the patient is desired.

Browning (1) and his co-workers, while investigating the relationship between constitution and bactericidal action among basic benzol derivatives, came to the conclusion that the dyes belonging to the acridine group possessed extremely powerful bactericidal and antiseptic properties, which are considerably increased when the dyes are mixed with blood serum. They also state that these dyes have power to stimulate phagocytosis and the growth of connective tissue. Ligat, (2), Wells (3), Carslaw and Templeton (4), Burchfiel (5), Davis (6), Peck (7), and many others report very favorable results obtained by the use of these dyes in the treatment of infected wounds and gonorrhea.

In this communication we shall report the results of our study with two flavine dyes, acriflavine and proflavine, in regard (1) to their inhibitory properties on the development of tubercle bacilli in culture media and (2) to their therapeutic value in infected animals. Our study was carried on only with the American dyes which we obtained through the kindness of the Heyl Laboratory, New York City. We cannot speak about the French or English preparations.

Acriflavine is 3.6-diamino-10-methyl-acridine-chloride and was originally prepared by Bunda at the suggestion of Ehrlich. It was found to have a marked therapeutic effect in trypanosome infections. The compound at first was called trypaflavine because of its trypanocidal action.

Proflavine is 3.6-diamino-acridine-sulphate, and is claimed by the maker to possess the same bactericidal properties as those of acriflavine but is less toxic when used for intravenous or other inoculations. The two dyes in question are not altered by heat; they are nontoxic when inoculated intravenously in a dilution of 1 to 1000; and are not precipitated by the addition of normal or stronger salt solution or sodium citrate.

INHIBITORY PROPERTIES

For the study of inhibitory properties on the cultivation of tubercle bacilli, the veal infusion of 4 per cent glycerin broth was used. The medium was prepared as usual. It is sterilized for three successive days in Arnold sterilizers and the following dilutions with the dyes ranging from 1 to 1000 to 1 to 1,000,000 were made, inoculated as usual by floating the growth on the surface of the culture media and incubated. The results obtained are recorded after a four weeks incubation:

DILUTION	DEGREE OF GROWTH	
	Acriflavine	Proflavine
1:1,000	No growth	No growth
1:5,000	No growth	No growth
1:10,000	No growth	No growth
1:25,000	No growth	Slight growth
1:50,000	Slight growth	Slight growth
1:100,000	Fair growth	Fair growth
1:500,000	Good growth	Good growth
1:1,000,000	Abundant	Abundant
Control	Abundant	Abundant

From the above table it is evident that the dyes in question possess inhibitory properties on the development of the tubercle bacilli. The acriflavine probably possesses a slightly higher degree of this property than the proflavine. In the former the dilution of 1 to 50,000 will inhibit the growth of tubercle bacilli, and in the latter 1 to 25,000. Incidentally, during this study we also found that Bacillus subtilis will develop in a dilution of 1 to 25,000.

ANIMAL EXPERIMENTATION

Our experimentation was only with rabbits and guinea pigs.

Twenty-four guinea pigs were injected subcutaneously with a light emulsion of human tubercle bacilli, isolated from the sputum of a patient, which in previous study was proved to be virulent for guinea pigs. After fourteen days the 24 guinea pigs were divided into three

TABLE 1

Guinea pig experiments. June 4, 1920. Pigs inoculated with 0.1 cc. suspension of virulent human tubercle bacilli

SERIES NUMBER	JUNE 21, 1920	JUNE 28, 1920	JULY 6, 1920	JULY 14, 1920	JULY 21, 1920	JULY 28, 1920	AUGUST 4, 1920	AUGUST 11, 1920	AUGUST 18, 1920	AUGUST 25, 1920	SEPTEMBER 1, 1920	SEPTEMBER 8, 1920	SEPTEMBER 15, 1920	DAYS OF LIFE	AUTOPSY
	cc.	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*		
Proflavine 1	2	2	2	2	2	2	2	2						73	August 16, 1920. Tuberculosis
Proflavine 2	2	2	2	2	2	2								58	August 1, 1920. Tuberculosis
Proflavine 3	2	2	2	2	2	2	2	2	2	2	2	2		97	September 9, 1920. Tuberculosis
Proflavine 4	2	2	2	2	2	2	2	2	2					76	August 19, 1920. Tuberculosis
Proflavine 5	1	1	1	1	1	1	1	1						74	August 17, 1920. Tuberculosis
Proflavine 6	1	1	1	1	1	1	1	1	1	1	1	1	1	108	September 20, 1920. Tuberculosis
Proflavine 7	1	1	1	1	1	1	1	1						69	August 12, 1920. Tuberculosis
Proflavine 8	1	1	1	1	1	1	1	1	1	1	1			90	September 2, 1920. Tuberculosis
Acriflavine 1	2	2	2	2	2	2	2	2	2					77	August 20, 1920. Tuberculosis
Acriflavine 2	2	2	2	2	2									49	July 23, 1920. Tuberculosis
Acriflavine 3	2	2	2	2	2									52	July 26, 1920. Tuberculosis
Acriflavine 4	2	2	2	2	2	2	2	2	2	2				83	August 26, 1920. Tuberculosis
Acriflavine 5	1	1	1	1	1	1	1	1	1	1	1			93	September 5, 1920. Tuberculosis
Acriflavine 6	1	1	1	1	1	1	1							67	August 10, 1920. Tuberculosis
Acriflavine 7	1	1	1	1	1	1	1	1	1					80	August 23, 1920. Tuberculosis
Acriflavine 8	1	1	1	1	1	1	1	1	1					79	August 22, 1920. Tuberculosis
Control 1														111	September 23, 1920. Tuberculosis
Control 2														89	September 1, 1920. Tuberculosis
Control 3														59	August 2, 1920. Tuberculosis
Control 4														123	October 4, 1920. Tuberculosis
Control 5														146	October 27, 1920. Tuberculosis
Control 6														96	September 8, 1920. Tuberculosis
Control 7														131	October 12, 1920. Tuberculosis
Control 8														104	September 16, 1920. Tuberculosis

Each cubic centimetre contained 0.005 gram of the dye.

groups of 8 each. Group 1 received weekly subcutaneous injections of the proflavine dyes in normal salt solution. Group 2 received weekly injections of acriflavine in salt solution, and the third group was kept for control.

It first was necessary to determine the proper dosage for animal experimentation. Browning found that when rabbits were inoculated with acriflavine, so that the dose represented 0.066 per kgm. of body weight, the blood serum of such animals, when diluted with an equal volume of normal salt solution, completely inhibited the development of staphylococci and Bacillus coli. Taking this as a basis and finding out by our experiment that a dilution of the dyes of 1 to 10,000 will completely inhibit the development of the tubercle bacilli, we decided to use the dyes in such a dilution that a dose represented 0.03 gm. of the dye for each kgm. of body weight. The average weight of all guinea pigs was 350 grams. (See table 1.)

Table 1 shows that the controls outlived the treated animals. The average lifetime of the animals which received proflavine was eighty days after the injection. The group that was treated with acriflavine lived seventy-five days, and the third group which consisted of the controls (not treated) outlived the treated ones; that is, their time of life was one hundred and seven days. It seemed to us that acriflavine was more toxic for guinea pigs than the proflavine. This experiment on guinea pigs was repeated and as the result was the same as the first experiment we shall not give the details.

RABBIT EXPERIMENTS

Twelve rabbits, having an average weight of 1200 grams, were injected intravenously with 0.2 cc. of emulsion of bovine tubercle bacilli, each microscopic field with the oil immersion having an average of eight tubercle bacilli. Two weeks after the injections the rabbits were separated into three groups. Eight rabbits were selected for treatment and the other 4 were the controls. Four of the 8 animals were treated with acriflavine and the other 4 with proflavine. Each treated animal received 30 mgm. of the dye in 10 cc. physiological sodium chloride solution. During the treatment the control animals gained weight while the treated ones gradually lost weight. (See table 2.) The above experiments were repeated, and as the results were practically the same as the first experiments, the details are omitted.

TABLE 2

Rabbit experiments. June 7, 1920. Rabbits inoculated intravenously with 0.2 cc. suspension of bovine tubercle bacilli

SERIES NUMBER	JUNE 24, 1920	JULY 2, 1920	JULY 9, 1920	JULY 16, 1920	JULY 23, 1920	JULY 29, 1920	AUGUST 5, 1920	AUGUST 12, 1920	AUGUST 19, 1920	AUGUST 26, 1920	SEPTEMBER 2, 1920	SEPTEMBER 9, 1920	SEPTEMBER 16, 1920	SEPTEMBER 23, 1920	DAYS OF LIFE	AUTOPSY
	cc.	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*	*cc.*		
Proflavine 9..........	10	10	10	10	10	10	10	10	10	10	10				92	September 7, 1920. Tuberculosis
Proflavine 10.........	10	10	10	10	10	10	10	10	10	10	10	10			100	September 15, 1920. Tuberculosis
Proflavine 11.........	10	10	10	10	10	10	10	10	10	10	10				94	September 9, 1920. Tuberculosis
Proflavine 12.........	10	10	10	10	10	10	10	10	10	10	10	10	10	10	115	September 29, 1920. Tuberculosis
Acriflavine 9.........	10	10	10	10	10	10	10	10	10	10	10	10			99	September 14, 1920. Tuberculosis
Acriflavine 10........	10	10	10	10	10	10	10	10	10	10					83	August 29, 1920. Tuberculosis
Acriflavine 11........	10	10	10	10	10	10	10	10	10	10					83	August 23, 1920. Tuberculosis
Acriflavine 12.........	10	10	10	10	10	10	10	10	10	10	10				93	September 8, 1920. Tuberculosis
Control 1............															116	September 30, 1920. Tuberculosis
Control 2............															93	September 8, 1920. Tuberculosis
Control 3............															107	September 22, 1920. Tuberculosis
Control 4............															128	October 2, 1920. Tuberculosis

Each 10 cc. injected for treatment represented 0.03 gram of the dye.

SUMMARY

1. Acriflavine and proflavine (American preparations) have inhibitory properties on the development of tubercle bacilli when these dyes are used in culture media. In the former this property is in a dilution of 1 to 50,000, and in the latter, 1 to 25,000.

2. The dyes as therapeutic agents in experimental tuberculosis are of no value, but have a tendency to accelerate the progress of the disease.

3. All controls outlived the treated animals.

I wish to thank Dr. Walter B. James for having suggested this study.

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A NEW AND EASY METHOD FOR THE DEMONSTRATION OF GRANULES IN TUBERCLE BACILLI[1]

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The tubercle bacillus is hard to stain; but when it has absorbed an aniline dye it does not discharge the color readily. Alcohol, acid, and alkali will decolorize the material containing the bacilli much more quickly than they will decolorize the bacilli; knowledge of this fact has been a great help in the investigation of the life cycle of the tubercle bacillus.

Many methods have been devised for the differential staining of tubercle bacilli and a few for the demonstration of granules, contained in or free from the bodies of the bacilli. Much in 1907 first described these granules and a method for their staining. Since then, other methods of staining them have appeared in the literature from time to time. The most important of these are:

Much's method and its modification by A. Kirchenstein; Von Betegh's method; Fontes's technique; Sesqueira's method; and P. Spehl's modification of Spengler's method.

These staining methods entail a rather prolonged and complicated technique. A method which would be quick and easy to use, and would show plainly the bacilli and the granules (in the bacilli or free), and would at the same time eliminate the confusion possible when other Gram positive organisms are present, would be very useful. The following staining technique provides these desired results:

Only three solutions are necessary beside the counterstain, the use of which is optional:

1. The staining reagent, which may be called Carbol-fuchsin-violet Solution, is

Carbol-fuchsin	four parts	by volume
Carbol-methyl-violet	three parts	

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[1] Read at a Monthly Conference of the Medical Officers of the Connecticut State Tuberculosis Sanatoria, at the Norwich Sanatorium, February 7, 1921.

(If the mixture shows a metallic scum, add 95 per cent alcohol drop by drop till the scum disappears.)

2. The fixing solution, which is a concentrated Lugol's solution, is

Iodine	1 gram
Potassium iodide	2 gram
Distilled water	100 cc.

3. The decolorizing solution, which can be called the A. A. A. Solution (acid, alcohol, acetone), is

Concentrated hydrochloric acid	10 cc.
Alcohol, 95 per cent	50 cc.
Acetone	40 cc.

(This gives a concentration of approximately 3 per cent HCl.)

The technique is as follows:

The smear is prepared in the ordinary way and fixed by heat; then

1st. Cover with carbol-fuchsin-violet and heat to steaming (do not allow to boil) for ½ to ¾ minute. Wash.

2nd. Cover with Lugol's Solution for 1 to 1½ minutes. Wash.

3rd. Cover with A. A. A. solution and renew till decolorized, from ¾ to 1 minute. Wash.

4th. If desired, counterstain with 1 per cent aqueous methylene blue. Wash, dry and examine.

A certain latitude in the different steps is allowable, thus making it very easy to obtain good results with this staining technique:

The staining in step 1 can be carried from ½ to 2 minutes.

The action of the Lugol's Solution can be carried from ½ to 4 minutes.

The decolorizing in step 3 is more within limits:— from ¾ to 1¼ minutes for smears of sputum and pus, and ½ to 1 minute for pure cultures; 1 minute and ¾ minute, respectively, being the best time. *It is best to make the smears thin enough to have complete decolorization in that time.*

The whole procedure takes about 2½ to 3 minutes and with ordinary care good results are obtained in every preparation, permitting easy differentiation between the granules (either in the bacilli or free), the bacilli themselves and other organisms present.

RESULTS

The granules are purplish-black.

The bodies of the bacilli are red or deep pink.

The other organisms and cellular constituents take the counterstain. *All Gram positive organisms other than tubercle bacilli stain the same color as the background.*

POSSIBLE VARIATIONS

Two variations of the above technique can be used if more convenient: In staining, step 1, one does not have to use an already mixed preparation of carbol-fuchsin and carbol-methyl-violet, but can put on the cold slide three drops of the latter for every four drops of the former, rocking the slide from side to side to mix them before heating.

Also, instead of Lugol's Solution in step 2, tincture of iodine can be used for the same length of time. The results are the same.

In experimenting with spore-forming organisms none have been encountered which did not completely decolorize; and different strains of smegma bacillus (acid-fast with Gabbett's Solution) almost totally lost the stain (red or purple) so that the error from that source is considerably minimized; and further study might prove this stain very useful in differentiating between the smegma bacillus and the tubercle bacillus in urine and other material.

CONCLUSIONS

The advantages of the above technique can be summarized as follows:

1. The small number of solutions, their stability and easy preparation with material obtainable in even small laboratories.
2. The speed and simplicity of technique.
3. The uniformly good results obtained.
4. The clear differentiation between the so called Much granules, the tubercle bacilli, and all other organisms and granules.

A CASE OF TUBERCULOMA OF LEFT FRONTAL LOBE OF BRAIN[1]

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The case is of interest because of the following points: (1) nature, size, situation of the lesion, and the age of the patient; (2) great number of convulsions; and (3) difficulty of harmonizing the neurological symptoms with the autopsy findings.

HISTORY

Mr. R., white male, aged thirty-four years, real estate agent.

Family History: No tuberculosis, or other chronic disease in family. Married; has three healthy children; a fourth has epilepsy.

Past history: Scarlet fever, 1900; rheumatism, 1902; influenza, 1918. Negative for venereal infection. Always strong and vigorous, worked hard, and was successful in business. Subject to headaches, especially in the evening, and did not sleep well. Habits good.

Thirteen months before the present illness, he returned from a fishing trip in the afternoon, and the same evening dined out. While telling a story, he was noted to have difficulty in finding his words, and immediately fell into a convulsion. A second convulsion occurred in half an hour, and a third within an hour. A nearby physician was called, who, after making a negative examination, offered the opinion that the attacks were of psychogenetic origin, as follows: The patient, fatigued by his travel, tripped in speech, was humiliated, and succumbed to a hysterical demonstration, the form of which was determined by memory of his child's epileptic seizures. His family physician leaned to the theory of a uremic origin, and kept the urine under observation for several months, though the findings were always negative. Recovery from the above was complete, and, aside from the headaches and insomnia above mentioned, he had excellent health.

Present illness: December 13, 1920, he returned from a hunting trip, apparently in excellent condition, except that he complained of a lame feeling in his right shoulder, which was attributed to the effects of carrying his gun.

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[1] Case and specimen presented before the Society for Nervous and Mental Diseases of the District of Columbia, February 17, 1921.

That night, after retiring, he had a convulsion. Next day he appeared well, and was out of doors interested in his children's play. At 3 A.M., December 15, he had another seizure, and the convulsions began to recur at regular intervals. It was estimated that about 20 attacks occurred before he was admitted to the George Washington University Hospital, which was effected at 10 A.M., December 15. The attacks recurred with regularity from this time to within an hour of his death, which took place December 17, at 11:55 A.M. The interval was at first about forty minutes, but it gradually shortened, until toward the end, they occurred every five minutes.

I saw the case with Dr. Luckett at eleven o'clock, the morning of the 15th, and twice the next day. Dr. Luckett testifies that in the interval between the earlier convulsions, seen by him at the patient's home, the patient appeared to make a normal recovery, speaking, moving, and acting as was his habit. The findings of my examination on the first visit were:

Convulsive cycle: Abrupt onset, with laryngeal stridor. Face drawn to the right. Seizure involves all the limbs, beginning with small movements like a coarse tremor. These rapidly become wider in amplitude, more violent, and slower in rate, consisting of a violent jerking, and involving the limbs of the right more than those on the left side. They gradually become less violent, slower, and cease, a period of relaxation following. The duration of the convulsion is thirty seconds to one minute or more. The attacks are accompanied by cyanosis, which rapidly passes when the convulsion is completed. During the convulsion the eyes and tongue are drawn to the right; the facial muscles are in tonic contraction, more so on the right; left extremities extended, and the right semiflexed. As the attack ceases, the breathing is stertorous, but this passes with the cyanosis.

Examination in intervals between convulsions: Patient is conscious, face congested. Right temporal artery very prominent. (His wife states that this has been the case for a long time.) Incomplete left facial paralysis. Complete flaccid paralysis of left arm and leg. Respiratory movements symmetrical. Speech lost, but he can understand what is said. Is able to protrude the tongue, and can swallow. *Eyes*: Subconjunctival hemorrhages. Pupils equal, and respond to light. Eyes swing slowly from side to side. Eye grounds somewhat hazy, but there is no hemorrhage, and the discs are normal. *Reflexes:* Abdominal: absent on both sides. Cremasteric: left diminished, right active. Patellar: left absent, right faint. Achilles: both absent. Plantar: left no response, right present. Babinski: left no response, right a lively positive. No Kernig on either side. No abnormalities found of heart, lungs, or abdominal viscera. *Urine:* acid; specific gravity, 1,025; albumen positive; sugar negative; many hyaline and granular casts, with a few leucocytes and red blood cells. *Spinal fluid*: Flows without increased pressure; is clear and colorless, cells per cu. mm., 6; globulin increased; Wassermann negative.

Progress: The pulse ranged from 100 to 116; respirations from 24 to 30; temperature from 100° to 101°F. There was a terminal rise of temperature to 103.4°. He complained of pain in the left frontal region. Control of the urine and feces was maintained till near the end, though there were at times involuntary urine and feces during a convulsion. Was able to take liquid diet till terminal coma set in. Bromides, chloral, chloroform inhalation and morphine had no effect in modifying the convulsions.

Diagnosis: The clinical diagnosis was that the patient had an intracranial lesion of long standing, with recent acute diffuse infiltration. Syphilis was excluded by the examination of the spinal fluid. Sarcoma was considered improbable, as it was unlikely that an intermission of activity of thirteen months would have occurred. The opinion was given that the disease was probably tuberculosis. Localization of the primary lesion was not made, but was assigned to a silent area.

Prognosis: was absolutely unfavorable, and an early fatal issue was predicted. Operative procedure was considered, but was rejected unless the clinical picture should change.

Autopsy (By Dr. O. B. Hunter): Abstract: On sagittal section of the left cerebral hemisphere, a large solitary tubercle was found in the anterior pole of the frontal lobe, involving the superior, middle and inferior frontal gyri, and extending well down in the corona radiata to within $\frac{3}{4}$ inch of the corpus striatum. It measures $1\frac{3}{4}$ inches in its sagittal diameter by $1\frac{1}{4}$ inches in the vertical, by 1 inch in the transverse. Superiorly and mesially it is covered by a very thin shell of cerebral cortex. Its central mass is composed of soft, gelatinous, hemorrhagic, necrotic material, with a rather firm, but somewhat eroded "motheaten" wall. Microscopic examination shows considerable hemorrhage, old and recent, some fibrin, large numbers of endothelial leucocytes and epithelioid cells, many round cells, and a few polymorphonuclear leucocytes. There are considerable granular debris and cellular detritus. A moderate number of tubercle bacilli is present.

Posterior to the above described tubercle, and occupying a similar position with respect to the frontal convolutions, $1\frac{3}{4}$ inches anterior to the proximal end of the fissure of Rolando, there is another area exhibiting induration, capillary engorgement and petechial hemorrhages, with slight necrosis. It is separated from the above described tubercle by a cortical peninsula of cerebral tissue, $\frac{3}{4}$ inch wide. This second area measures $\frac{3}{4}$ inch in its sagittal diameter, $1\frac{1}{4}$ inches in its vertical, and $1\frac{1}{4}$ inches in its longest transverse diameter. It is continuous at its anterior-inferior border with the first described tubercle, from which it is elsewhere separated as described above. Microscopic sections show the same pathological changes as are described for the first lesion. There is considerably less hemorrhage and fibrin, but large numbers of endothelial leucocytes and epithelioid cells are present, with a moderate number of round cells, and a scant number of polymorphonuclear leucocytes. Granular debris and cellular detritus are present, but are more or less scattered in separate foci. Tubercle bacilli (few) are present.

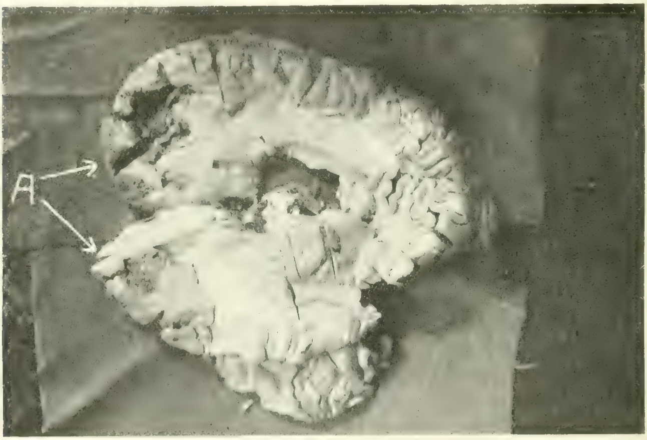

FIG. 1. SAGITTAL SECTION THROUGH LEFT HEMISPHERE, 1 INCH FROM LONGITUDINAL FISSURE

Mesial portion upright; temporal portion reflected downward in foreground. *A* indicates tuberculoma. Formalin fixation.

The cellular accumulations in both instances are thrown together in a more or less haphazard fashion, and there is no evidence of any tendency to the formation of tubercle, giant cells, or fibrosis.

There is marked engorgement of all the cerebral veins, and hemorrhagic extravasation over the region of the left Sylvian fissure, extending over the left temporal lobe and fissure of Rolando; slight basilar meningitis and adhesions of pia at anterior pole of left temporal lobe; evidences of old basilar meningitis in region of anterior and posterior perforate spaces, and over corpora mamillaria. The dura is adherent in the region of parieto-occipital sulcus, and also over both right and left cunei. No other focal lesion found.

A few old healed nodules were found in the apex of right lung. No other pathological changes except terminal congestion of organs.

Diagnosis: Tuberculous encephalitis (*solitary tubercle of left frontal lobe*).

SUMMARY

During the patient's stay in the hospital, 10:30 A.M., December 15, to 11:55 A.M., December 17, 278 convulsions were counted. It was estimated that there were 20 seizures the morning of the 15th before his arrival at the hospital. That is, there were a little short of 300 convulsions within eighty-one hours.

The distribution of the paralysis, left hemiplegia, including the lower segments of the left facial distribution, suggested a capsular lesion. No capsular lesion was found on the right side, except vascular engorgement. During life no satisfactory examination of the sensory system could be made, because of the aphasia, and the brief period between the attacks. The spinal cord was not removed at the autopsy. Therefore, a clinico-pathological exclusion of a lesion of the spinal tract is lacking. However the inclusion of the facial nerve in the paralysis makes such a lesion improbable. But supranuclear paralyses are, as a rule, spastic in type. Is it possible that the rapidly recurring convulsions so exhausted the paralyzed muscles, that they could not respond to the afferent stimuli that ordinarily produce spasticity?

TUBERCULOSIS OF HUSBAND AND WIFE[1]

A REPORT OF 150 CASES

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The statistical material on which this article is based was obtained from the records of 5608 consecutive cases of tuberculosis admitted to the Rhode Island State Sanatorium between November 1, 1905, and May 5, 1921. There were 2262 married persons admitted, and of these, 62, or 2.7 per cent, claimed to have partners suffering from pulmonary tuberculosis. Of the 62 cases, 12 were repeated admissions of the same patients, leaving 50 different individuals. The elimination of duplicate admissions from all married cases, it is believed, would have made no material change in the percentage of patients with tuberculous consorts (2.7 per cent).

Of these 50 married patients with tuberculous consorts, 29, or 58 per cent, had tubercle bacilli in the sputum and the remainder had symptoms and signs which were considered diagnostic. Eight of the 50 patients had consorts who were patients in this institution, and, in the remaining cases, the patients' statements that their consorts were tuberculous were unverified by the institution. That 2.7 per cent of all tuberculous patients should have tuberculous consorts is not surprising, as 2.7 per cent of the general population probably has clinical tuberculosis. Assuming that tuberculosis is transmitted between married partners, it should not be expected to be evident in a few days or weeks, as do diseases ordinarily classed as contagious, because the massive doses likely to transmit infection are usually given late in the disease and the consort receiving the infection may not develop recognizable disease for one, two, or three years, or until after the death of the partner first affected.

Statistics based on patients who have had consorts die of tuberculosis are more valuable, not only because plenty of time may elapse for the development of the disease, but also because death is something definite. Patients' statements that their consorts died of consumption, like the physicians' certificates, on which they are usually based, are subject to occasional error and are, therefore, inferior to autopsy records; yet they probably minimize, rather than exaggerate the number of cases of tuberculosis.

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[1] Read at the Thirty-eighth Annual Meeting of the American Climatological and Clinical Association, Lenox, Massachusetts, June 4, 1921.

Of the 5608 admissions, there were 277 widowed persons, and, if we exclude from the latter number 48 duplicate admissions, there are left 229 different individuals who had been widowed. Our records show 100 different persons whose consorts died of tuberculosis, but as 7 of these had subsequently been remarried and were classified as married on admission, and as there was no record kept of widowed persons whose consorts died of nontuberculous diseases and who subsequently remarried, these 7 remarried widows are excluded, leaving 93, or 40 per cent, of all widowed tuberculous persons who lost their consorts by tuberculosis.

Of the 100 dead consorts, 57 were husbands and 43 were wives. Of the 100 widowed tuberculous patients whose consorts were alleged to have died of tuberculosis, 71 had positive, and 29 negative sputum. Of the 29 having negative sputum, 12 had had hemoptyses, 7 of the remaining had had pleurisy, 2 of the remaining had had night sweats, and the 8 remaining patients had signs and symptoms which were held to be diagnostic. Seventy-seven of the widowed patients gave the period of time which had elapsed between the death of their consorts and their admission to the sanatoruim, and these periods averaged 4.5 years. In 23, or 30 per cent, the period was more than five years.

Of over 3400 deaths among married people under seventy years of age in Providence in the three years 1915 to 1917, inclusive, the deaths from tuberculosis were 11 per cent in 1915, 13 per cent in 1916, 12 per cent in 1917, and averaged 12 per cent for the whole period. In other words, the percentage of those widowed by tubercuolsis is over three times as great among our sanatorium patients as in the general community.

These statistics tend to show one of the following alternatives:

1. That this sanatorium attracts more than the normal ratio of persons widowed by tuberculosis.

2. That unfavorable conditions in the home contribute heavily to the development of tuberculosis in both consorts.

3. That tuberculosis is communicated from a tuberculous to a healthy consort.

The efforts of the public health nurses are greatest in the homes where there has been a death from tuberculosis and those who have lost a consort are more likely to seek early diagnosis. On the other hand, these statistics were about the same before there was enough public health work to affect the result. Equal pressure from the medical profession and nurses is put on all known tuberculous patients, whether widowed from tuberculosis or not, and for over four years no patient, however advanced, has been refused admission.

While it may be admitted that wives widowed by tuberculosis may be subjected to more hardship for a year or two preceding the death of their consorts than those widowed by other diseases, it would hardly be expected to make so great a difference as has been shown.

Arguments against the frequency of adult infection based on the low tuberculosis incidence among employees of institutions for tuberculosis are far from conclusive, not only because these employees exercise precautions against contamination by sputum not efficiently exercised in the home, but because the relations of husband and wife, such as sleeping in the same bed, kissing, etc., greatly enhance the danger; and also because the employees in most tuberculosis institutions live under a regimen which frequently arrests tuberculosis after manifest development.

Failure to infect animals a second time with tuberculosis, a few months or a few years after the first inoculation, hardly warrants sweeping conclusions as to the protective immunity conferred on the majority of adults by childhood infections. Proof that animals cannot be reinoculated with tuberculosis twenty, thirty or forty years after the first inoculation, would have value. The experiment of adult infection is, however, being carried out throughout the country by married partners, one of whom has tuberculosis, and the determination of the incidence of tuberculosis morbidity and mortality of those who have had consorts die of tuberculosis is more conclusive than animal inoculation. It is a subject of such vital importance to the tuberculosis movement that it merits exhaustive study by many workers in different localities.

CONCLUSIONS

1. The histories of 229 consecutive widowed patients admitted to the Rhode Island State Sanatorium, 1905 to 1921, show that 93, or 40 per cent, lost their consorts by death from tuberculosis, a tuberculosis mortality over three times that of the married people of the community.

2. Immunity from many diseases is short lived and until much more convincing evidence of permanent immunity against tuberculosis conferred by childhood infections is forthcoming, a cautious logic will not accept the confident statements that are being made as to the impossibility or rarity of adult infection.

MALNUTRITION AND ITS RELATION TO TUBERCULOSIS

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In my sanatorium experience of nearly fifteen years, I have seen the pendulum swing slowly but steadily from the adult toward the child in our endeavor to prevent and cure tuberculosis. We long ago realized that patients must be found in the incipient stage of disease if we are to be successful in effecting the greatest number of cures. In the effort to find the incipient cases we followed the trail and found that it led back to childhood. There we discovered the period when infection occurs and the transition from infection to incipient disease frequently takes place. I believe that a really incipient case of pulmonary tuberculosis in an adult is an extremely rare condition to find. The so called early cases in adults are in reality a reactivation of childhood disease.

To continue our former policy of waiting for pulmonary tuberculosis to become manifest in the adult before attempting its cure is a sad waste of effort. We must go further and stop the supply at the source. The recruits are being prepared and made ready from the files of children, as they advance each year to take the places of the maimed and fallen in the ranks of tuberculous adults. We must stop this recruiting before we can win the battle.

In order to get some data upon malnutrition and its relation to pulmonary tuberculosis, I arranged with the superintendent of schools in Westfield to allow me to make some physical examinations of the children who were found to be underweight. The work of weighing and measuring was done by the nurses employed by the Hampden County Tuberculosis Association, and they assisted in the subsequent examinations and made home visits when it was thought necessary to obtain information about living conditions.

At the Westfield school which was selected for examination there were 659 pupils. They comprised the ages that are found grouped in the kindergarten, first, second, third and fourth grades. The results of weighing and measuring showed 71.6 per cent normal, 15 per cent from 7 per cent to 10 per cent underweight, and 13.4 per cent as 10 per cent or more underweight. The total number of underweight children was 186, or 28 per cent of the whole number. Written consent was obtained to make physical examinations of 146. Twenty-two others from the normal weight group were referred to us because of some physical defect that the teachers had noted. None of these, however, showed any evidence of pulmonary disease. This made a total of 168 who were given complete examination.

Dr. Frederick Clark, a laryngologist, made a thorough examination, using the digital method to detect adenoids. He found that nearly all the children had diseased or enlarged tonsils and adenoid growths of some degree. Many were in need of immediate operation to relieve obstruction to breathing and to prevent impairment of hearing.

Dr. Bethell, the sanatorium dentist, examined the teeth of all the children and found that they had on an average eight carious teeth and that very few had ever had any dentistry done.

Dr. Morgan and I made all the chest examinations. We found 83 to have signs and symptoms indicating enlarged bronchial lymph nodes or changes in respiration that are often early manifestions of tuberculosis in children. Some of these symptoms were doubtless due to diseased conditions of the throat and nose.

Twenty of the children had a temperature of 100° or more at the time of the examination. This febrile condition might be transient or be due to any active disease or acute infection. As a check on the group under observation I had the nurse take the afternoon temperatures in one of the fourth grade rooms. The number of pupils was 44. Two children had a temperature of 99.8°, one 99.6°, five 99.4°, five 99.2°, seven 99°, a total of twenty with a temperature between 99° and 99.8°. It would seem, therefore, to be a safe conclusion that, when a child has a temperature of 100° or more, it is due to some pathological condition. Such a case should be followed up to determine whether the fever is frequent or persistent, and if so endeavor to find the cause.

The 83 children were examined again about two weeks later, and a more painstaking study of their lungs was made under quiet conditions. This time we eliminated all but 48. All the children in this group showed definite impairment of resonance between the scapulae and extending upwards toward the apices. The d'Espine sign was pronounced. The breathing was of a bronchial type. The physical signs were such that a diagnosis of tuberculosis affecting the bronchial nodes and structures about the root of the lungs would be warranted when found together with malnutrition and other symptoms of toxemia. Twelve of these children were later taken to the sanatorium for X-ray examination. The films confirmed our findings and showed that a diagnosis of tuberculous disease in its incipient stage would be justified.

The children attending this school came almost exclusively from Bohemian, Polish and Lithuanian families. The grades were the kindergarten, first, second, third and fourth. The percentage of malnutrition was 28 per cent. Another school of 240 pupils, from the fifth to the eighth grades inclusive, where the older children from the same families attended, showed 68 per cent of malnutrition, which was by far the highest of any school in town. The apparent reason for this great difference in nutrition in children of different age groups from the same families may be due to the fact that the older children are expected to work as much as possible in addition to their attending school, and also that they get little or no milk. The limited amount of milk that is provided in these homes is given to the younger children.

Is malnutrition an etiological factor in tuberculosis? It would seem from the results of the examination of these school children that the two were closely allied. We know that tuberculosis causes malnutrition. May not malnutrition itself also prepare the way for the implanted tubercle bacilli that are present in most children to become active and produce tuberculous disease?

COMMENT

The number of malnutrition cases in this school was 186; 146 of this group were examined and 48, or 33 per cent, were found to be definitely tuberculous.

The average percentage of malnutrition among the 2828 children that make up the school census in nine of the Westfield schools is 32 per cent. If the law of averages holds true then fully one-third of this number of children suffering from malnutrition have diseased bronchial nodes, which is the first step in the development of pulmonary tuberculosis. Furthermore, 48 cases in one school of 659 pupils is a little over 7 per cent of the entire number. While it is not justifiable to draw too many conclusions from so small a number of children examined, it is significant that this percentage of diseased children coincides closely with the present death rate from tuberculosis, which is also not far from 7 per cent. We may assume, however, that a large percentage of these 48 children will eventually break down and develop active tuberculosis and many of them will die before they are twenty-five years old, unless they have exceptionally good care and good luck.

The evidence I have submitted only goes to confirm the belief held by many observers that antituberculosis activities should be directed more and more toward child welfare. To cover such a vast field and get thousands of tuberculous and potentially tuberculous children under supervision we should strongly advocate the adoption in every city and town of a method of group instruction and individual treatment along the lines developed by Professor Emerson in his nutrition clinics for delicate children. This can best be done in connection with the schools, as the children are there brought under official control for ten months of each year. We are neglecting our opportunities if we fail to do extensive preventive work with these children when they are in the earliest stage of disease and at a period in their lives when they will respond most quickly to rational changes in diet and habits of living. We must improve the physique and build up strong, disease resisting bodies during childhood. Then the cases of tuberculosis, that smoulder away during adolescence only to break forth later on and decimate the ranks of young manhood and womanhood, will become fewer and fewer, and as a cause of death in the next generation this disease will become a much less important factor.

TUBERCULOSIS IN DISCHARGED SERVICE MEN

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A great deal of attention is being paid to the recognition, by means of clinical signs and symptoms, of pulmonary tuberculosis in its less advanced stages, and the consequent possibility of instituting treatment before the prognosis has become too grave. Pottenger has done a great deal in calling attention to, and explaining the mechanism of, these clinical findings. This question will not be discussed at all in this paper; Pottenger's works are referred to, for this purpose; and they contain a full bibliography of other writings on the subject.

The following observations were made on discharged soldiers and sailors, who were examined as applicants for compensation under the War Risk Insurance Act. As a rule, the cases were available for study for a day or two at most, during which a thorough physical examination was possible. In case of necessity they were detained for a longer period of study. It must be kept in mind that in this series, advanced cases of tuberculosis, or of other diseases, did not occur very frequently, since they had been weeded out by the discharge examinations: those who could not pass the latter were detained at military hospitals for treatment.

The purpose of these observations is to study the relative importance of the various physical and subjective findings in the diagnosis of pulmonary tuberculosis. Data have been obtained from the following material:

Total number of men examined in one year		800
Number of diagnoses of tuberculosis		58
Number in series analyzed		50
Omitted from analysis		8
Tuberculous hip, no chest findings	2	
Tuberculous peritonitis, no chest findings	1	
Advanced tuberculosis of the lungs	2	
Previous diagnosis of tuberculosis; no findings now	3	

In order to secure uniformity and thoroughness in the examinations, an outline form was used. A representative selection of clinical signs and symptoms was made, and printed in full on the sheet. Findings were indicated by checking or underlining when positive, and crossing out with a line through the words, when negative or not elicited.

The clinical findings, can be classified, from the standpoint of their use in diagnosis, according to table 1.

The first group in the table consists of the effects of tuberculous toxins on the system. These effects are more or less common to all infections, varying in number and severity according to the amount and duration of the infection. The absence of these symptoms in a case of tuberculosis is practically equivalent to a lack of activity of the pathological process.

The second group consists of a number of phenomena, particularly discussed by Pottenger, resulting from the reflex effects along the peripheral nerves, due to visceral stimulation of the corresponding spinal segments. An inflammation at the apex will cause such a constant bombardment of the nerve cells in the segment corresponding to the visceral branches from the apex, that the outgoing stimuli find their way along all the efferent nerves from that segment; consequently skin segments, muscles, and sensory segments are affected, with production of pain and paresthesias, atrophy of the skin, and tension, hypertrophy and atrophy of muscles. These phenomena, referred to an apex or a hilum, denote the presence of an inflammatory process. Lesions other than tuberculosis are so rare at the apex, that an apical process may be considered practically synonymous with tuberculosis.

The third group requires no discussion; it consists of the old classical findings of consolidation, cavity formation, and cough with sputum containing signs of disintegrating lung tissue.

It will be noted that cough is listed in both the second and third groups of table 1. The reflex cough is the slight, dry, brassy cough, occurring very early, and seldom noted by the patient himself, but usually reported by his friends. The productive cough occurs when there is actual disintegration of lung tissue, with the presence of debris in the bronchi which must be got rid of.

Similarly, hoarseness falls into two categories. The hoarseness produced by actual local tuberculous infection of the larynx is not considered in this discussion. The hoarseness mentioned in the second group is a reflex phenomenon. Irritation of the recurrent laryngeal nerve by mediastinal infiltration explains some cases, but not all.

TABLE 1

Toxic symptoms	Indicate an infectious process. Not peculiar to tuberculosis. Alone, do not necessarily indicate tuberculosis. In connection with other signs indicate degree of activity of the process
Weakness and early fatigue	
Poor appetite	
Afternoon fever	
Loss of weight	
Night sweats	
Dyspnea	
Reflex symptoms and signs	Indicate an inflammatory process in the lung; most of them refer to the apex. Consist of peripheral nerve stimuli from spinal segments that supply visceral nerves to the lung. Reference of tuberculosis from these signs depends on the rarity of other lesions in the apex
Hoarseness and cough	
Frequent colds	
Gastrointestinal symptoms	
Constipation or diarrhea	
Pain in the thorax	
Shoulder droop	
Concave shoulder crest	
Prominent clavicle	
Sloping clavicle	
Hilum dimple	
Deficient expansion	
Apex	
Base	
Spinal deformity	
Muscular tension	
Flattening of chest	
Skin sensitiveness	
Local symptoms and signs	Indicate infiltrative or destructive process in the lung. Differentiate from bronchiectasis, pulmonary abscess, chronic bronchitis, pneumonia, empyema, etc.
Hemoptysis	
Pleurisy	
Cough with expectoration	
Increased vocal resonance	
Increased whispered resonance	
Diminished percussion resonance	
Unilateral narrowed isthmus	
Moisture in apex	
Bronchial breathing	
Râles	
Specific signs	An occasional acid-fast bacillus on a slide does not necessarily mean an infection
Tubercle bacilli in sputum	
X-ray	

A diagnosis of tuberculosis was made on the basis of the presence of important signs and symptoms belonging to the toxic, reflex, and local groups. The presence of the specific group was not considered essential. If the diagnosis could be checked up by specific findings,

TABLE 2

Signs and symptoms in order of frequency of occurrence

	NUMBER OF CASES	PER CENT
Early fatigue	39	78
Diminished resonance in apex	39	78
Loss of weight	37	74
Râles, moisture, or both	34	68
Cough	32	64
Abnormally prominent clavicles	30	60
Afternoon fever	28	56
Malaise	27	54
Night sweats	25	50
Restricted expansion of apex	25	50
Poor appetite	23	46
Tachycardia	23	46
Pain in thorax	23	46
Dyspnea	23	46
Râles	22	44
Bronchial breathing	21	42
Unilateral narrowed isthmus	20	40
Increased whispered resonance	18	36
Moisture	18	36
Increased vocal resonance	16	32
Constipation	14	28
Gastrointestinal symptoms	12	24
Shoulder droop	12	24
Restricted expansion of base	12	24
Hoarseness	10	20
Lagging	10	20
Hemoptysis	8	16
Nervousness	8	16
Scoliosis	8	16
Increased muscle tension	8	16
Unilateral flattening over apex	7	14
Pleurisy	6	12
Hilum dimple	4	8
Frequent colds	3	6
Sloping clavicle	3	6
Unilateral skin hypersensitiveness	3	6
Diarrhea	2	4
Concave shoulder crest	2	4
Kyphosis	2	4

it was that much more certain. However, when specific signs are present, the process is already considerably advanced; and our endeavor is to make a study of the diagnosis of the process before such an advanced stage is reached.

The diagnosis was not made unless all three groups were represented, except in one case, which lacked reflex findings. This case had been diagnosed as tuberculosis in a military hospital, pronounced arrested, and now showed signs of renewed activity.

The occurrence of the clinical findings in order of their frequency in the fifty cases, is given in table 2.

It will be noted that there is no symptom or sign which was present in every case. Conversely, it may be stated that there is no sign or symptom which is essential to a diagnosis of pulmonary tuberculosis. On the contrary, one must endeavor, from the findings which are present, to form an estimate of the pathological process which causes them. It may safely be stated that no two cases present the same picture.

The first fourteen items listed contain the entire toxic group; no toxic symptom is present in less than 46 per cent of the cases. Table 3 states in a different way the greater importance of the toxic group.

TABLE 3

GROUP	NUMBER OF SYMPTOMS INCLUDED	NUMBER OF TIMES FOUND IN SERIES	"CONCENTRATION" OF THE GROUP IN THE SERIES
Toxic	6	175	29
Reflex	16	180	11
Local	10	200	20
Specific	2	27	14

The number of times each group occurred, divided by the number of symptoms represented in each group, gives the figure in the last column of table 3. The toxic group predominates. The main significance of this is that the patient is sick. The pathological changes must be localized by means of other findings. It is my opinion that afternoon fever would have been found in a greater number of cases if there had been opportunity to study all the cases over a greater length of time.

In explanation of table 4, it may be said that the number of symptoms included in a group is purely arbitrary with the examiner. Therefore, the total number of times a group occurs, cannot be taken as representing its importance, for, in that way, a group with a large number of items, such as the reflex group, would readily predominate over one with a small number of items, such as the laboratory. Therefore, the total number of times a group occurred is divided by the number of items in the group, giving the average number of occurrences per group.

Diminished resonance in the apex has a maximum frequency of occurrence. It must be emphasized that in eliciting this sign, very light percussion must be used. The elements in the percussion sound are the vibration of the chest wall and the vibration of the pulmonary air. In incipient cases, we are searching for a small area, the consistence of which has changed only very slightly. Heavy percussion will vibrate a large portion of the lung, and obliterate all slight changes in the response of the tissues to the stroke. The change in the percussion note is due to alterations in the tone of the tissues of the chest wall, as well as to change of consistency in the lung itself. Only delicate percussion and a finely trained ear can bring out these small differences.

TABLE 4

SYMPTOM GROUP	NUMBER OF SYMPTOMS IN GROUP	NUMBER OF TIMES FOR THE GROUP	AVERAGE NUMBER OF TIMES PER SYMPTOM
History	18	343	19
Inspection	10	103	10
Palpation	2	11	5
Percussion	3	71	27
Auscultation	6	129	21
Laboratory	2	27	13

Symptoms arranged in order of frequency of occurrence:

Percussion
Auscultation
History
Laboratory
Inspection
Palpation

In this series of examinations, the fine, subcrepitant crackling, brought on during an inspiration following a complete emptying of the alveoli, has been differentiated from coarser, more clearly distinguished râles. The percentage of cases in which one or the other or both of these findings occurred is 68; this can therefore be considered as an important finding. But it will be noted that it is by no means essential. The absence of râles or moisture will not necessarily rule out tuberculosis from the diagnosis.

The percentage of occurrence of cough is given as 64; I think that this would be higher if the patients could be observed more closely, or the accounts of their friends obtained. The slight reflex cough of early tuberculosis often goes unnoticed by the patient himself.

Scoliosis and kyphosis are fairly frequent findings. These do not include cases in which actual spinal caries or arthritis were present; no such cases are included in this series. The cases reported represent only those in which loss of tone in the muscles of the back has caused a slight deformity; or an inequality of the muscle action, increased tone here and decreased there, has drawn the vertebral column out of its normal shape. I consider this an important diagnostic sign.

In making the comparisons suggested by table 5, it must be kept in mind that the personal equation of the internist and the roentgenologist making the examination exercises some influence on the exact figures.

TABLE 5

X-ray examinations of the chest, 21 cases

The percentages which follow are based on the number of cases in which both physical and X-ray examinations were made:

	NUMBER OF CASES	PER CENT
Physical and X-ray diagnosis agreed exactly	15	71
Active by physical and inactive by X-ray	4	19
Agreed on positive diagnosis without reference to activity	19	90
Active by physical and negative by X-ray	2	9
Active by X-ray and negative by physical	0	0

TABLE 6

Occurrence of tubercle bacilli

	NUMBER OF CASES	PER CENT
Tubercle bacilli found in sputum	8	16
Sputum negative for tubercle bacilli	19	38
No sputum	23	46
Tuberculosis indicated by sputum, not by physical examination	0	0

We all realize that arriving at a diagnosis from a physical examination does not hang definitely on sharp distinctions; it consists of a verdict arrived at, after weighing the evidence pro and con. We sometimes lose sight of the fact that an X-ray diagnosis represents the same process; it is mentally in no way different from a physical diagnosis, based on an opinion derived from the consideration of objective findings. A case pronounced negative by the X-ray and positive by physical examination may be interpreted in any of the following ways: Roentgenologist failed to find or interpret signs actually present on the plate; internist too enthusiastic; both off the track; or, as I have done in this case, physical signs if carefully sought and interpreted with the proper training, may, in individual cases, appear before the pathological process in the lung is sufficiently advanced to produce any change in the X-ray shadow. It will be noted that the converse, failure to find physical signs in a case pronounced positive by the X-ray, has not occurred in this series.

Table 6 merely confirms the old maxim that a negative finding in sputum examination for tubercle bacilli means nothing, even though frequently repeated; a positive finding checks up our diagnosis. This latter statement must, however, be somewhat qualified. A single acid-fast bacillus, or even an occasional one, is by no means a certain proof of pulmonary infection. An all-night search of a slide by the interne, and the triumphant finding of a single red bacillus, is by no means the triumph that it may seem. Acid-fast bacilli, nontuberculous, occur in tap water and in the mouth. Tubercle bacilli may be present in the mouth and throat, with or without the presence of local infection, and in the absence of pulmonary infection. Artefacts may closely resemble tubercle bacilli; knowledge of the morphology and grouping of the organism is necessary to be certain of the diagnosis.

The above table also calls attention to the fact that not even the presence of sputum is essential in making the diagnosis. In fact, the presence of sputum, unless referable to an intercurrent bronchitis, means a case considerably advanced.

The percentages of previous history and family history are probably much smaller than they would be, if the actual facts could be ascertained. A patient will remember if he has been told by a physician that he has tuberculosis; but he will not remember various symptoms that might have occurred in the past, indicating a flare-up of a chronic condition. These conditions are probably more frequent than we at present believe, recovering spontaneously, or under treatment for something else; and only those sufficiently susceptible progressing to an advanced stage. For that reason, especially, I believe that the treatment of an advanced case is a fight against unequal odds, representing, as it does, a patient who has susceptibility greater than most of us. Exceptions to this statement will be found in cases contracting the disease after unusual exposure, such as that presented by military life.

The family history is also incomplete, as it was not possible to interrogate anyone except the patient himself in any of the cases.

In regard to the influenza cases, two aspects are apparent. Our modern conception of the tuberculous individual considers him as carrying the infection in a latent state, ever since his childhood. Very often, he is just a little below par physically; his resistance is not what it ought to be. He is the very first one to contract any infection that comes along. On the other hand, the extreme prostration following cases of influenza can readily be understood as causing a flare-up of

TABLE 7

Previous history and family history of tuberculosis

	NUMBER OF CASES	PER CENT
Previous history of tuberculosis	11	22
Family history of tuberculosis	2	4
Previous illness (possible relation to etiology)		
Influenza	10	20
Pneumonia	7	14
Gassed	6	12
Cerebrospinal meningitis	2	4
Associated conditions		
Otitis media, chronic	3	6
Tonsillitis	2	4
Organic heart disease	2	4
Rheumatism (chronic arthritis)	2	4
Chronic peritonitis (tuberculous?)	2	4
Pes planus	2	4
Sinusitis, frontal and ethmoidal	1	2
Tuberculous lymph nodes of the neck	1	2
Cold abscess of the rib	1	2

TABLE 8

Leading symptoms

	NUMBER OF CASES	PER CENT
1. "Weakness," malaise, early fatigue	12	24
2. Pain in the chest	10	20
3. Productive cough	5	10
4. Loss of weight	5	10
5. Gastrointestinal symptoms	5	10
6. Hemoptysis	3	6
7. Discovered during course of routine examination	3	6
8. Hoarseness	3	6
9. Pain and weakness in back	2	4
10. Headache	1	2
11. Previously diagnosed	1	2

mediastinal infection, which otherwise might never have been disturbed. The only influence that can be ascribed to the other diseases, mentioned in the table, is that of lowering the general resistance.

Table 8 presents the leading symptoms in order of frequency of occurrence:

These are the causes that actually impelled the patient to seek medical help. The first four are suggestive of tuberculosis, even to the lay mind, and the doctor usually examines the lungs carefully when a patient complains of them. Gastrointestinal, nasopharyngeal and neurotic symptoms should become just as definitely suggestive in the physician's mind of tuberculosis, as are cough and emaciation.

TABLE 9

Results of treatment

	NUMBER OF CASES	PER CENT
Lost track of	25	50
Treated	16	32
Sanatorium	3	6
Improved	1	2
Not improved	2	4
Home	13	26
Improved	11	22
Not improved	2	4
Worse	0	0
Not treated	9	18
Improved	1	2
Not improved	5	10
Worse	3	6

While it is not the aim of this paper to discuss treatment, table 9 is presented to show what can be done, even under unfavorable circumstances. It was impossible for me to control any but a very few of these cases. My influence over them was not that of a physician over a private patient; owing to the amount of work the office entailed, I was unable to become intimately acquainted with every man, I was limited by the formalities of the service in carrying out some of the measures I should have desired; and it was especially difficult to get patients to continue treatment. They were usually interested in securing compensation and, when this was achieved, their interest in my office ceased.

Only in one case is improvement of an untreated case shown. However, it is interesting to speculate what would be the result of an investigation of the 50 per cent that passed from observation. The very fact that they were no longer heard of, suggests that a considerable percentage of them experienced no further trouble. This would be expected *a priori* in accordance with the modern idea, that tuberculosis is a condition common to most of us, but is rapidly progressive in only a few (in reality very many) exceptionally susceptible cases. Careful observation is gradually bringing out the fact that this chronic condition occasionally flares up, and again subsides.

In conclusion it may be said that physical examination is the most important of the methods at our disposal for the recognition of early tuberculosis of the lungs. Physical examination increases in value with the increasing skill of the examiner. It is a method which requires long and patient practice. The delicate percussion stroke, the hearing of the slight crackling due to moisture, the detection of slight differences in skin tone and muscle tension, cannot be accomplished by an examiner attempting it for the first time. Yet, it is worth cultivating; it means the detection of cases early enough to benefit them by treatment.

THE MUSCULATURE OF THE FINER DIVISIONS OF THE BRONCHIAL TREE AND ITS RELATION TO CERTAIN PATHOLOGICAL CONDITIONS[1]

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It is not the purpose of the present paper to enter into a detailed description of the bronchial tree; only so much as is necessary to elucidate the topic under consideration will be outlined.

The trachea divides into the right and left bronchus which, with their branches, are distributed to the right and left lung. On the right side the bronchus divides into three principal branches which correspond to the normal lobation of the right lung; on the left side the bronchus divides into two principal branches which correspond to the lobation of the left lung. Variations from this normal division are of frequent occurrence. Followed deeper into the lung it will be found that bronchi of the second, third, and fourth orders can be recognized; these are followed by bronchioli of various orders, and last of all by the ductuli alveolares (alveolar ducts).

The musculature of the trachea and of the carina tracheae have been described elsewhere by the author. There remains for consideration the musculature of the cartilaginous bronchi and bronchioli, and that of the noncartilaginous bronchioli and of the ductuli alveolares. For the present the musculature of the cartilaginous bronchi and bronchioli will be passed over, for it presents problems peculiar to itself; only the musculature of the noncartilaginous bronchioli and of the ductuli alveolares together with its relation to the parenchyma of the lung will be considered.

The earliest description of the musculature of the bronchi was given by Reisseisen. He described it as being attached to the bronchial cartilages and spreading out so as to fill the spaces between the cartilages. The muscle did not disappear at the point where the cartilages ceased to be present; but it could be followed by means of a dissecting lens, especially in the lungs of an adult, robust man, as far as it was possible to open a bronchial tube with a scalpel. Reisseisen inferred from this that it extends to the ultimate end of the bronchial tube. Because he gave the primary description of the bronchial musculature, later investigators have frequently called it the *Muscle of Reisseisen.*

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[1] The greater part of this work was accomplished through the aid of a special fund furnished by the National Tuberculosis Association.

Following Reisseisen there is a long list of investigators who have made mention of the muscle and have given various descriptions of its arrangement. From this list the descriptions given by the following authors have been selected as the best representatives of the diverse opinions.

E. Schultz describes the muscle as forming a completely closed layer. Frankenhäuser describes the muscle as a *Ringmuskelschicht,* which forms in the human lung a muscular tube with only occasional breaks in its continuity. F. E. Schulze describes the muscle as consisting of smooth muscle fibres that pursue a circular course; but he adds that toward the end of the terminal branch, the layer gradually grows thinner and finally breaks up into individual ring bands, which are separated from each other by more or less broad fissures. These bands often consist of only a single layer of muscular cells, but are at the same time interwoven with delicate elastic fibres which traverse them at right angles.

Toldt gives a more detailed description of the muscular layer. He describes the muscle as forming a completely closed layer in the bronchi of the cat; but the walls of the bronchi in man also have smooth muscle bundles in their entire circumference. They are situated just beneath the tunica propria of the mucosa and form a connected but not a complete layer. Their arrangement is lattice-like (*gitterförmige*), as can be best demonstrated in bronchi which have been cut open and spread out flat. The muscle is arranged in flat bundles, which have, in general, a nearly transverse course and unite to form a network. Between these bundles there are spaces, bounded by acute angles, which are situated transverse to the long axis of the bronchi. When the bronchi are cut transversely the muscle layer appears here and there to be interrupted and the smooth muscle bundles are cut, not in a true longitudinal direction, but more or less obliquely. In the smallest interlobular bronchi the muscle bundles are thin, and consist of only a few cells and are much further apart; however, they still surround the entire circumference of the bronchial tube.

Sappey describes the muscle as being continuous, and compares it to the circular layer of muscle in the intestinal wall. The latest study of the bronchial musculature is that of Dubreuil and Lamarque. They studied the musculature of the bronchi in the human lung and that of various domestic animals. They give an illustration of the network of smooth muscle in an "alveolar canal" from the lung of an ox. The muscle is described as a plexiform sphincter and, according to their illustration, the rather coarse mesh of the network is elongated parallel to the long axis of the alveolar duct. They support the statement made by Rindfleisch that muscle is present in the walls of the air sacs and alveoli.

In the following study use has been made of the lung of the guinea pig, the cat, the dog, and man. Figure 1 shows a section from the lung of a guinea pig in which a cartilaginous bronchiolus, 0.165 mm. in diameter, is cut in such a plane that the muscle bands are divided somewhat obliquely, while in one of its branches, 0.125 mm. in diameter, only a portion of the upper segment of the bronchiolus is included in the section, and this shows the bands of muscle arching over the wall of the bronchiolus.

The bands have an average thickness of 0.03 mm., and they vary from 0.01 mm. to 0.0265 mm. in width. The bronchiolus is contracted and this accounts for the close approximation of the bands. A careful examination of the microphotograph will, however, show the branching and anastomosing of the muscle bands. The lung of the guinea pig contains, proportionally, a larger amount of smooth muscle than that of any other animal I have studied. It is the presence of this large amount of muscle in the bronchial tree and in the pleura that makes the lung of the guinea pig so difficult to distend.

Figure 2 is a photomicrograph of a section of a noncartilaginous bronchiolus, 0.65 mm. in diameter, from the human lung. The plane of the section is such that the muscle bands are seen extending across the lower wall of the bronchiolus. These bands are not as closely applied to one another as those in figure 1, because the bronchiolus is extended and not contracted; this permits the branching and anastomosing of the bands of muscle to be more clearly seen. The bands vary from 0.02 mm. to 0.03 mm. in thickness and from 0.008 mm. to 0.05 mm. in width.

In the lower portion of the figure the muscle bands are obscured by the extensive pigmentation. It was on account of the large amount of

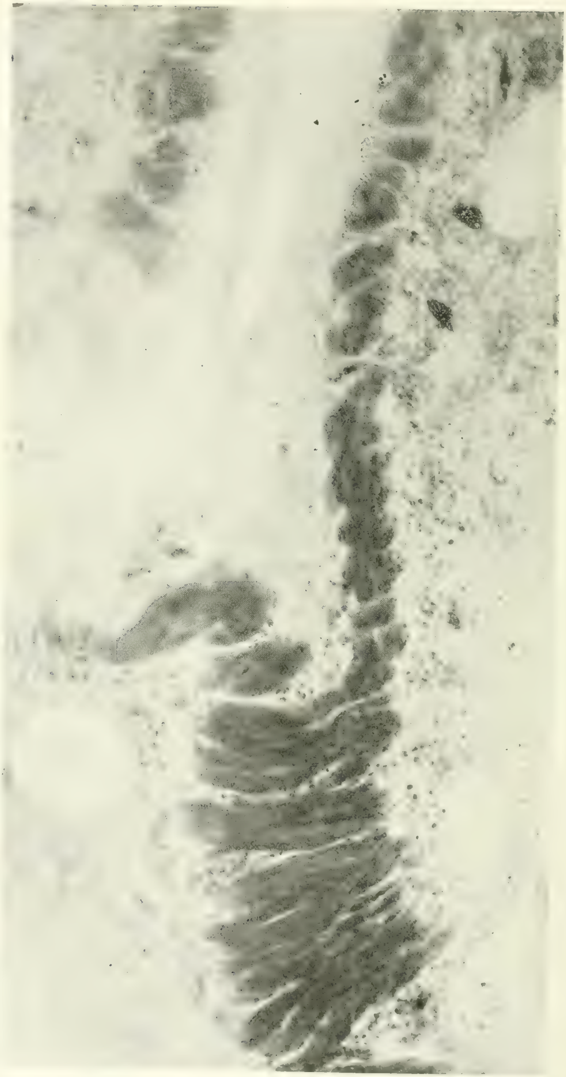

FIG. 1. MUSCLE BANDS IN A BRONCHIOLUS FROM THE LUNG OF A GUINEA PIG. × 120

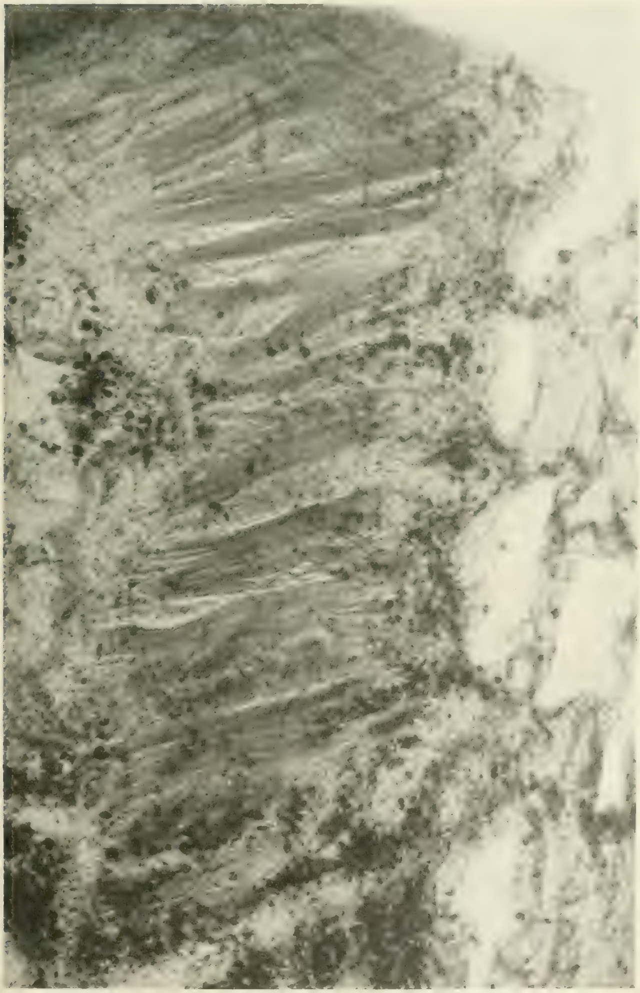

FIG. 2. MUSCLE BANDS IN A BRONCHIOLUS FROM THE HUMAN LUNG. × 120

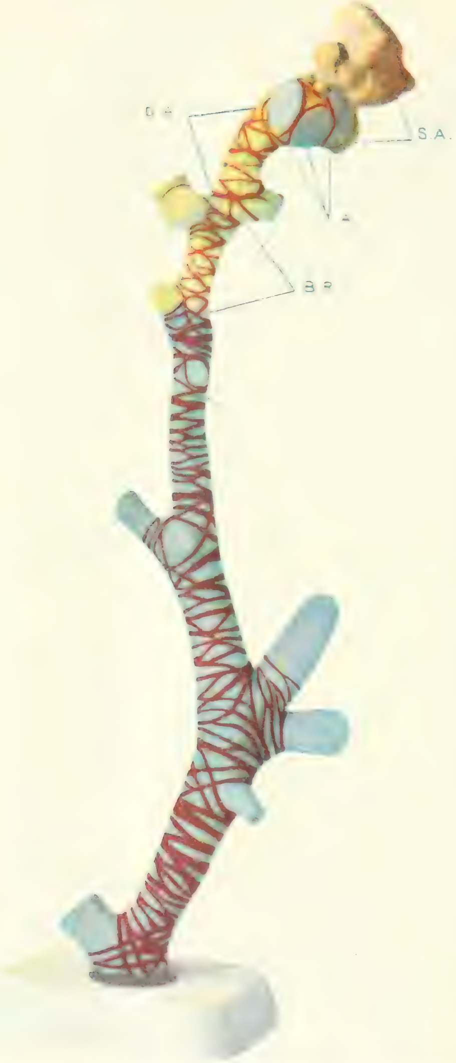

FIG. 3. RECONSTRUCTION OF A BRONCHIOLUS WITH ITS MUSCLE, AND ITS SUBDIVISIONS, FROM THE LUNG OF A DOG

B. R., Bronchiolus respiratorius. *D. A.*, Ductulus alveolaris. *A.*, Three atria, two of which have been cut off; a fourth atrium does not appear in the photograph. *S. A.*, Air sacs, one of which has been cut off. × 125 and reduced to 10.

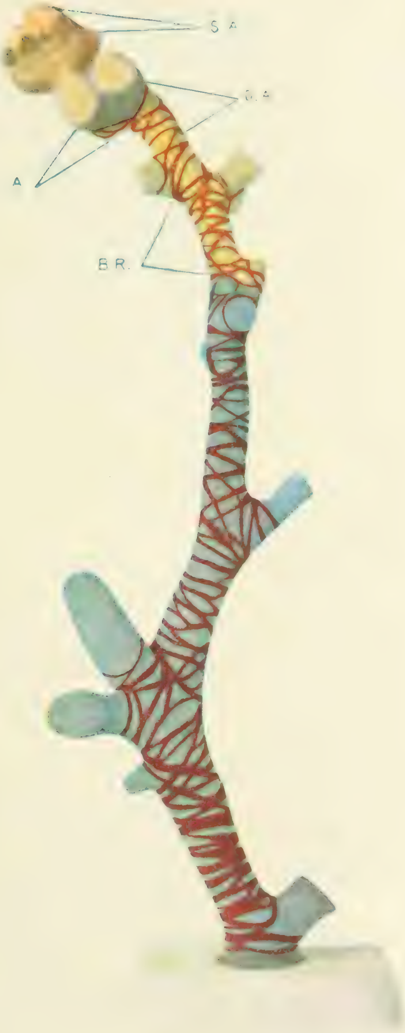

Fig. 4. Same Reconstruction as Figure 3

See legend accompanying figure 3

pigmentation present in such human lungs as were available that the study was transferred to the dog's lung. Numerous comparative studies have shown that there is practically no difference in the arrangement of the muscle in the two lungs.

Figures 3 and 4 show two views of a reconstruction, from a dog's lung, of the musculature of a noncartilaginous bronchiolus, 0.565 mm. in diameter, its branches, and its termination in a primary lobule (anatomical unit), of which only a single air sac is shown completely reconstructed. All of the muscle bands were drawn by means of the camera lucida and placed on the model in as near their original position as possible. By this method the width of the muscle bands, their thickness, their relation to each other, their relation to the places where branches were given off from the bronchiolus, and the distance to which muscle extended in the lung was ascertained.

As was the case with the bronchiolus illustrated in figure 2, this bronchiolus is extended; it is in the condition of full inspiration. The angle at which the muscle bands diverge from each other shows a marked contrast to those in figure 1 and it also shows the advantage of studying the lung in the condition of full inspiration. The tendency of the muscle bands to have more or less of a triangular arrangement at the place where branches are given off is easily made out in both figures 3 and 4. This arrangement is quite characteristic and has, probably, a direct relationship to the arrangement of the elastic fibres at this point. The problem which this arrangement opens up cannot be discussed at the present time; it is being worked out by one of my students and the results will be reported in detail at some future time.

When the subdivision of the bronchiolus *B. R.* (figs. 3 and 4) is reached the character of the bronchiolus changes. Up to this point its walls have been intact, but now alveoli push their way between the muscle bands, which form a sphincter about their opening into the bronchiolus, and give the bronchiolus a nodular appearance. The presence of these alveoli along the bronchiolus occasions the name *bronchiolus respiratorius* to be given to this portion of the bronchiolus; that is, a bronchiolus which takes part in the act of respiration and has alveoli opening out from its lumen.

That portion of the bronchial tree situated distal to the bronchiolus respiratorius (*D. A.*, figs. 3 and 4) is known as the *ductulus alveolaris* and is the last division of the bronchial tree. Each ductulus alveolaris and the air spaces into which it breaks up constitute the anatomical unit (primary lobule) of the lung. A ductulus alveolaris differs from a bronchiolus respiratorius in that it is of smaller diameter, and has a greater number of alveoli connected with it which, like the alveoli connected with the bronchiolus respiratorius, have a sphincter-like arrangement of muscle about their opening into the ductulus alveolaris.

Authors, in general, fail to distinguish between an alveolus belonging to a bronchiolus respiratorius or to a ductulus alveolaris and one belonging to an atrium or to an air sac. The former is an alveolus which communicates with the lumen of an air tube and, because of the arrangement of the muscle bands, has a greater or less amount of muscle in the knob, inverted T, or head of a cane shaped wall which forms the boundary of its opening into the air tube. *The muscle belongs to the air tube and not to the alveolus.*

In individual sections which have been cut in such a plane as to include the alveoli of an air tube, but not the air tube itself, it is not improbable that the presence of muscle has led to the statement that muscle is present in the walls of the air spaces. The same may be true of alveoli belonging to air sacs which abut against a bronchiolus when they are cut in such a plane that only the muscle of the bronchiolus is included in the section. This has probably led to the statement that muscle bands penetrate to the bottom of the alveoli. Keeping in mind the fact that the "infundibulum" of the older authors included an atrium and an air sac, the conditions outlined above explain the statement made by Rindfleisch that "the circular bundles of the muscular fibres of the smallest bronchioles send into the orifice of the infundibula some partial prolongations which penetrate to the bottom of them." If, however, serial sections are made use of (and they should be in studying the structure of the lung) the proper relation of the muscle will at once be recognized.

At the distal end of the ductuli alveolares the bands of muscle (best seen in fig. 3) form a sphincter about the openings leading into the atria. These sphincters undoubtedly play an important role in asthma. In normal respiration the opening is of such a size that the air passes unimpeded in and out of the atria and air sacs. When, however, contraction of these muscles takes place the size of the opening is much reduced. The muscles of inspiration reduce the intrathoracic pressure and permit the air to rush with considerable violence into the air spaces and they become distended. Due to the narrowing of the opening, the air can not be emptied from the air spaces as readily as under normal conditions.

A larger amount of residual air than normal remains. With each succeeding inspiration more air accumulates and the air spaces become still further dilated. The muscles of expiration are not as powerful as those of inspiration and the normal elasticity of the lung being overcome, the air accumulates behind the contracted opening leading into the atria. It is not improbable that there is also a tonic contraction of the muscle in the walls of the bronchioli respiratorii and ductuli alveolares which causes a reduction of their lumina. With the relaxation of the contracted muscle, the opening dilates and, the air flowing out freely, the overdistention of the air spaces is relieved and the attack is almost instantaneously over.

Distal to the sphincters about the openings leading into the atria, no muscle was found. As stated when describing the muscle about the alveoli opening out of the bronchioli respiratorii and ductuli alveolares, the muscle bands which form these sphincters belong to the musculature of the bronchial tree and not to the atria.

In longitudinal sections of those bronchioli which are found in the fibrous scar tissue of "healed tuberculosis" at the apex of the lung, where the apex has contracted, small herniae of the mucosa lined with columnar or cuboidal epithelium are often seen. If studied carefully, it will be found that at the point where one of these herniae breaks through the wall of the bronchiolus, there is, on either side, one of these muscle bands cut transversely. The hernia has broken through at the point of least resistance. In transverse sections of the bronchioli they are not as readily recognized as in longitudinal sections. These herniae constitute, in one sense of the word, the beginning of a bronchiectasis, not the tubular dilatation, but the sacular dilatations that sometimes present a bead-like appearance along the course of the bronchioli and are the starting point of those cavernous spaces which open into the lateral wall of a bronchiolus.

Figure 5 is a diagrammatic outline of a median section through the reconstruction shown in figure 3, and gives the diameter in millimetres of its various divisions. At the lower end of the bronchiolus, where it is 0.565 mm. in diameter, the muscle bands are 0.022 mm. in thickness; in the ductulus alveolaris, which measures 0.192 mm. in diameter, the muscle bands are 0.013 mm. in thickness. While the bronchiolus has diminished about 65 per cent in diameter, the muscle has diminished only about 43 per cent in thickness. These results follow closely those obtained by Grancher, who found that in bronchi 10 mm. in diameter

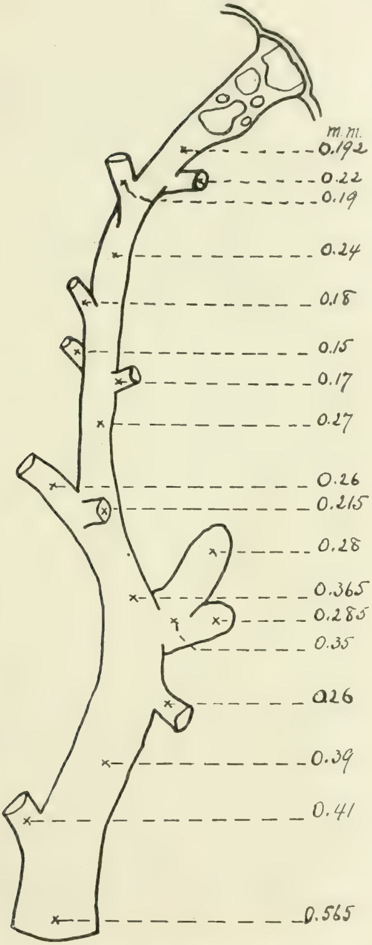

FIG. 5. DIAGRAMMATIC SECTION THROUGH FIGURE 3

Diameter measurements given in millimetres the muscle was 0.2 mm. in thickness, while in bronchioli 1 mm. in diameter the muscle was 0.1 mm. in thickness. In other words the muscle bands were five times as strong in a bronchiolus 1 mm. in diameter as in a bronchus 10 mm. in diameter.

In a series of sections of an injected dog's lung, which was cut after the reconstruction was completed, the section shown in the photomicrograph, reproduced as figure 6, was found. It is of interest in that it shows nearly all of the divisions of the bronchial tree that enter into the reconstruction. If the curve of the two be compared (figs. 4 and 6) it will be found that they correspond quite closely. With a strong reading glass a few of the muscle bands situated in the lower wall of the bronchiolus can be made out.

The arrangement of the muscle bands, as described above, suggests an explanation of certain changes which occur in the bronchial tree during expiration and inspiration. In figure 7, photographs of Wood's metal corrosions of the lower right lobe of the lungs of two dogs, of the same size and weight, are shown. In *B*, the lung was completely collapsed. The injection mass penetrated only a short distance into the lateral and dorsal branches of the main stem bronchus from which they are given off at an acute angle. Both the main stem bronchus and its branches have the appearance of being somewhat increased in diameter; this is especially noticeable in the main stem bronchus. In *A*, the lung was placed in a glass jar and the air was exhausted. When the lung was in the condition of full inspiration Wood's metal was injected. Not all the air spaces were filled with the injection mass. This incompleteness, however, makes the corrosion all the more interesting, for it permits a better insight into what has taken place with the dilation of the air spaces. When compared with *B*, it will be seen that the angle formed by the lateral and dorsal branches with the main stem bronchus has been greatly increased. This increase of the angle provides space for the expansion of the air spaces and, as a result, it can be seen that some of the smaller bronchioli with their atria and air sacs have been filled with the injection mass. Not only has the angle at which the branches leave the main stem bronchus become wider, but both the branches and the main stem bronchus have also elongated and become somewhat reduced in diameter.

When the mechanism of inspiration is taken into consideration we find an explanation of the changes which have been noted in connection with the bronchi and bronchioli. With the descent of the diaphragm

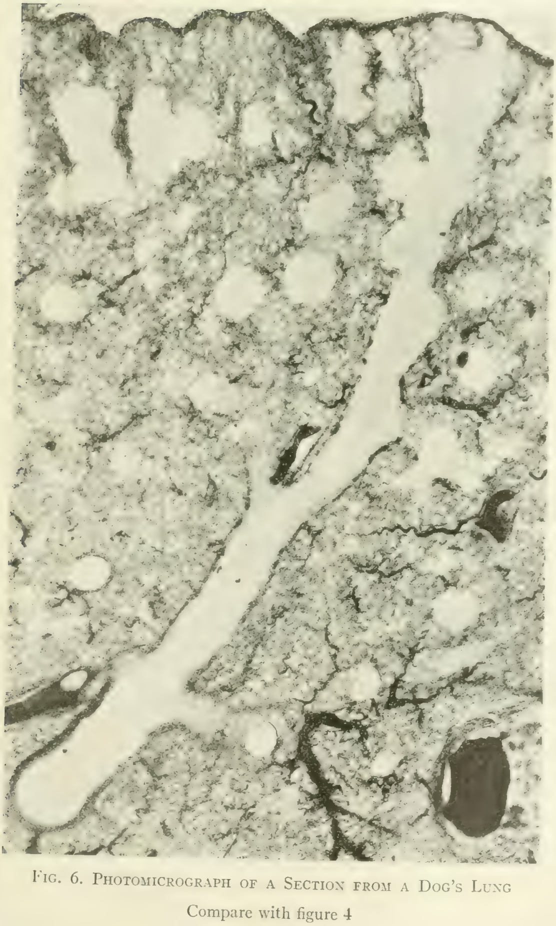

FIG. 6. PHOTOMICROGRAPH OF A SECTION FROM A DOG'S LUNG

Compare with figure 4

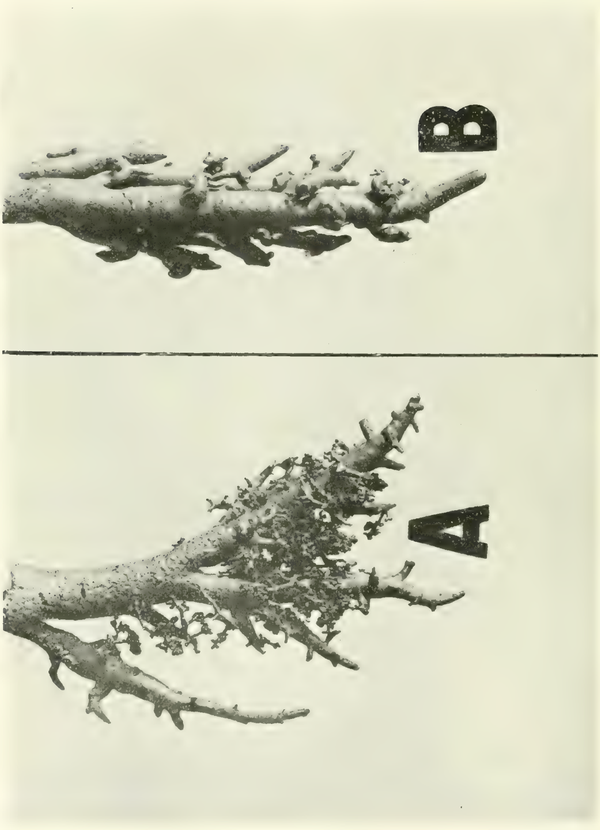

Fig. 7. Wood's Metal Corrosions from the Lungs of Two Dogs

A, In full inspiration. *B*, In collapse and the expansion of the inferior aperture of the thorax the lungs have followed the downward movement of the diaphragm and the pressure of the outside atmosphere has caused an influx of air, which has filled the airspaces that have been emptied to a greater or less degree by the normal elasticity of the lung and by the shutting together of the bronchi and bronchioli. It has seemed from a study of a number of corrosion preparations that there is a greater amount of expansion, proportionally, along the diaphragmatic surface of the lung than at the apex. Just how much difference there is cannot be stated at present; the subject needs further study.

When the action of these bands of muscle is studied it will be found that the arrangement is such that provision is made for the elongation of the bronchi and bronchioli during inspiration and the subsequent shortening during expiration. The movement may be roughly compared to that which takes place in the opening and closing of the so called "lazy tongs," the anastomosing bands forming a geodesic network.

If figure 1 be compared with figures 3 and 4, the changed relationship of the muscle bands in a contracted bronchiolus and in an extended bronchiolus can be readily seen. That the action of the bronchial musculature in expiration is not passive, but active, seems quite clear, and its action in regulating the tension of the air within the atria and air sacs deserves much more attention than physiologists have given to it.

SUMMARY

The bronchial musculature is not arranged in the form of distinct bands which encircle the bronchi and bronchioli, neither is it in the form of a continuous sheet, but it is in the form of a network. This network is made up of geodesic bands which prevent any tangential motion, and in this way provide for the greatest amount of strength and at the same time permit the greatest amount of extension and contraction of the bronchioli and their subsequent subdivisions.

The muscle bands form a sphincter about the openings of the alveoli into the bronchioli respiratorii and ductuli alveolares; they also form a sphincter about the openings leading into the atria. These bands belong to the musculature of the bronchial tree and not to the air spaces.

Distal to the openings leading into the atria no muscle has been found. There is no muscle in the walls of the air spaces.

The size and position of the lungs is constantly changing with the respiratory movements. If the condition of the lungs at the end of a normal expiration be taken as a starting point it will be found that in the act of inspiration they increase in extent, especially that portion of each lung that is directly influenced by the descent of the diaphragm. This increase in size has its influence on the bronchial tree and especially on the smaller bronchi, the bronchioli, and their subdivision.

In extreme expiration the dorsal and lateral branches form an acute angle with the main stem bronchus, while in inspiration they open out, the angle becomes wider and at the same time they elongate. This change is necessary in order that provision may be made for the expansion of the air spaces.

The action of the bronchial musculature in expiration is active rather than passive.

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CHEMICAL PROBLEMS IN THE BACTERIOLOGY OF THE TUBERCLE BACILLUS[1]

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An able investigator, Dr. Kendall, once defined bacteria, or partially defined them, as chemical reagents. The characterization is by no means far fetched, as we see when we stop to consider the multitude of reactions carried out sharply and completely by different bacteria, reactions duplicated exactly by ordinary analytical methods with common chemical reagents in the laboratory Consider the phenomenon of deaminization. If I add to the substance alanine, which has an amino or NH_2 group in its structure, a small amount of nitrous acid and warm the mixture, nitrogen is split off and a hydroxyl group substituted. The process is deaminization. The same end result may be secured through the action of a great variety of bacteria. Just how they accomplish the result we do not know. We speak somewhat vaguely of enzyme action, with notions far from clear on intermediate steps; yet the end result we know with certainty.

Take for another example the production of histamine from histidine. The latter is an amino acid and like all amino acids contains a carboxyl or COOH group. Under the action of some bacteria, notably certain strains of B. coli, CO_2 is split off and imid-azol-ethylamine produced, histamine, one of the most potent poisons known. Some of the same product may be produced from histidine in the laboratory by the simple process of dry distillation, CO_2 being split off at the high temperature.

Or consider the action of common yeast on dextrose. Through the enzyme action of the yeast we have produced—if we agree with Neuberg—pyruvic acid and atomic hydrogen. From the former, carbon dioxide is evolved with the production of acetaldehyde, which in turn is reduced by the aforesaid hydrogen with the production of ethyl alcohol,—no mean accomplishment for any chemist these days.

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[1] Read at a joint session of the Clinical and Pathological Sections, at the Seventeenth Annual Meeting of the National Tuberculosis Association, New York City, June 16, 1921.

Now much as I respect the analytical powers of bacteria I am more profoundly impressed by their aptitude for the reverse process, synthesis, their power of building up complex structures from the simplest of materials. I think of them as chemical machines especially adapted for synthesis on a grand scale. Of course, this ability is common to all forms of life from a baby down, but the process is followed more readily in the simple unicellular forms. The characterization as chemical machinery for synthesis holds for parasites and saprophytes, the difference in the two being entirely in their reaction to environment. If I may attempt a definition, too, I will say that a parasite is a mixture of proteins, capable of synthesizing more protein within the tissues of a living being; protein being the substance, according to the best information available at the present time, characteristic of life; and the rapid construction of that protein by small masses of the original protein constitutes virulence, chemically considered.

Unfortunately we are unable to catch any of the midstages in this remarkable process, although we can detect a good many in the reverse process, that of tearing down a protein molecule. We are able to set up a chemically well defined meal before a given bacterium, and determine with a high degree of accuracy what it takes and what it leaves, and then we are able to analyze the product and say—with far less accuracy—what it has done with what we provided. But how it put the structure together from the simple substances we gave it remains a puzzle.

I have been interested for some time in the utilization of certain food stuffs by the tubercle bacillus. Here is an organism that takes *us* for its food material and builds up its peculiar proteins out of the disintegration products of our proteins. I shall never forget how deeply impressed I was, when I was assisting in the work at the Reception Hospital at Saranac Lake, at the phenomenon of a twenty year old girl bringing up a quart of sputum a day, every one-twelfth oil immersion field of which contained hundreds and hundreds of living tubercle bacilli. There was synthesis, and parasitism, and virulence.

Now what is this tubercle bacillus, whose capacity for synthesis is so destructive to the human host? Chemically considered it is a mixture of proteins, nucleoproteins, and perhaps lipoproteins and glycoproteins, in a cell which contains a high amount, as compared with other bacteria, of certain peculiar lipoids. Because of this characteristic high fat content and its relation to the phenomenon of acid-fastness, an enormous amount of work has been done on this phase of the chemistry of the organism, and, I think, in proportion to the time, effort, and money spent on it, with the least success. Not that much good work has not been done, or that good men have not attacked the problem. I simply mean that lipoids are physically of such consistency that most of them have never been separated sharply, and purified and identified. But I have high hopes in this direction. Dr. Levene, who has done such splendid work in this field recently, tells me that we may look forward to the elaboration, within a very few more years, of methods which will make the analysis of lipoid mixtures a fairly exact procedure. In the meantime we have of course acquired much valuable information, even if it is far from complete. We know that the waxy mixture contains a good deal of true fat, and a high proportion of an alcohol of high molecular weight, called "mykol" by Sakae Tamura, and that phosphatids are present in considerable amount. I want to know more about these last substances, the phosphatids. I believe that the phosphorus problem has been highly neglected in bacterial chemistry in general. Here is a field which must be carefully cultivated when the new methods arrive.

I should like to take a vote in this audience to see how many consider the tubercle bacillus of plant, how many of animal nature. I have had it in mind for some time to apply certain chemical tests to this organism, to gain information on this perhaps academic point. As you all know the chemical distinction between plant and animal life is far from absolute; yet there are some lines on which broad generalizations on differences have been laid down. One of these respects the insoluble carbohydrates. In plants, the woody forms of life, we have such substances as cellulose, hemicelluloses and starch. In the lower forms of animal life, insects, crustaceans, etc., we have, in the hard parts, carbohydrates made up just as in plant life from polymerized small molecules, but with this difference,—that they contain nitrogen. In them, not glucose molecules as in starch, but glucosamine molecules, are piled up to make what is known as chitin. Now chitin has been described in several bacteria. Iwanoff was among the first to detect it, noting its presence in several forms, including the anthrax bacillus. As good a man as Ruppel, whose early article on the proteins of the tubercle bacillus is classic, suggests that chitin or a similar substance might be responsible for the acid-fastness of the organism. Helbing believed the same thing. The evidence was poor. But there is a problem to be worked out at any rate. Of course everything under the sun has been referred to as responsible for the phenomenon of acid-fastness, in almost total neglect, it seems to me, of the well known fact that an extremely finely powdered mass of tubercle bacilli ground, let us say, in a ball mill, is non-acid-fast. Presumably such a mass contains the same chemical constituents as the unground bacilli. The phenomenon of colloidal dispersion of the different constituents has not been thoroughly taken into account. The problem should be attacked by the physical as well as the organic chemists.

The protein of the tubercle bacillus has been considered essentially nucleoprotein. I think more or less inaccuracy has been involved in the decision, although there is no question that a good deal is nucleoprotein. But the test for nucleoprotein has too often been the presence of phosphorus in a crude protein mixture having the solubility characteristics of known nucleoproteins. In this connection I may say that just the other day in my laboratory we found a substance in defatted tubercle bacilli, which was rich in phosphorus, was soluble in water and alcohol, insoluble in toluene and acetone, and which was organic and gave a mercury salt, but gave none of the protein reactions. I was looking at the time for alcohol soluble proteins, which at the present time, because of the work of Osborne, are attracting considerable attention.

Some months ago, instead of using phosphorus as the indicator for the amount of nucleic acid present, I used substances far more definitely characteristic of nucleic acid, namely, the purine bases, and from the amounts found calculated that the nucleic acid content of the bacillus was between 2 and 3.5 per cent of the dry weight. This was smaller than I expected, and led me to believe that a higher proportion than I had originally supposed was simple protein. Through the coöperation of that excellent chemist, Dr. Treat B. Johnson, I expect to have another check run on this, using not the purine bases this time but other substances also highly characteristic of nucleic acid, the pyrimidine bases. Further data on a point I mentioned a few moments ago may be furnished by this investigation. Curiously enough, as far as we know now, there are two distinct nucleic acids and just two, one of these being found in plant forms, like yeast and wheat, the other occurring in animal tissues, like pancreas or thymus gland, the chromosomes of animal nuclei in general presumably. They are a good deal alike. The structure is the same. Each is built upon phosphoric acid linked with two pyrimidines and two purines by carbohydrate bridges. The purines are the same, guanine and adenine, but the pyrimidines vary and the bridge is different. Both forms are said to contain the pyrimidine cytosine, but in the plant acid the other pyrimidine is apparently uracil, while in the animal form it is thymine. And the carbohydrate bridge is in the plant acid a pentose, and in the animal a hexose. Now I am going to have the nucleic acid of the bacillus more thoroughly investigated. Through the courtesy of Parke, Davis & Co. and Mulford & Co. and Dr. Dorset of Washington, I have collected about three kilograms of dry tubercle bacilli, which are to be analyzed for certain things. Dr. Levene has promised to get out the nucleic acid and determine if its sugar is a pentose or a hexose, in series with his other valuable reports on nucleic acids. Dr. Johnson will supervise the work of a reliable pyrimidine chemist, who also will get out the nucleic acid and determine what pyrimidine bases are present in it. I may say that the presence of thymine has been recorded by several investigators, and cytosine and uracil have been looked for, but the results are incomplete and confusing.

There is desire for much investigation on the proteins present, because, of course, the phenomena of hypersensitiveness are the result of protein sensitization. It seems ridiculous that having known that fact for years we have so far failed to devote much attention to learning of what type those proteins are. We know the qualitative composition, to a certain extent, of the hydrolyzed proteins—Tamura has furnished us with a list of some of the amino acids present—but we do not know what the particular types of proteins present are. I plan to use some of my six pounds of tubercle bacilli on this problem.

Leaving the subject of the chemical composition of the tubercle bacillus for one with which I have more personal acquaintance, I would like to say something about the metabolism of the tubercle bacillus and some other acid-fast organisms. One of the best leads I know about in this field was furnished fifteen years or more ago by Theobald Smith, who noted that in the cultivation of tubercle bacilli on glycerol broth the media went through first an alkaline, then an acid phase. These changes have not been accurately accounted for chemically; partly, I believe, because we have used too complex media for the purpose. Commercial peptone is a hopeless mixture of things, and meat extract is much worse. I am engaged at the present time in running Theobald Smith curves on media of simple, known chemical composition, and trying now to understand the first or alkaline phase. I can think of just three ways in which culture media, glycerol-peptone broth, let us say, can become alkaline as the result of bacterial growth. One is by the splitting of amino acids or acid amides, which of course make up the bulk of peptone, into ammonia and an organic acid, with destruction of the acid or its incorporation into bacillary substance, and excretion, or at least slower utilization, of ammonia, leaving a preponderance of this substance in the medium.

The second is by the decarboxylation of these amino acids, carbon dioxide being driven off and alkaline substances, the amines, being left. This theory was quite attractive to me two years ago, because at that time I believed the tubercle bacillus would grow on methyl and ethyl amines as sources of nitrogen, and thought that it might be by this amine route that the corresponding amino acids, namely glycocoll and alanine, were broken down. I have since concluded that those results were due to impurities, chiefly ammonium chloride, in the preparations, and that the tubercle bacillus will not grow on amines, and that therefore these are probably not evolved in its katabolism of the amino acids of its food supply. The point is one of considerable importance, as the amines are very potent substances, physiologically considered. Take some examples. In the suprarenal gland we apparently have the amino acids, tyrosine and phenylalanine, decarboxylated and otherwise slightly modified and converted into the highly active epinephrin. At least one investigator believed that the hypophysis decarboxylates some of the histidine which reaches it and turns back into the blood stream the very important substance histamine. If the tubercle bacillus is one of the decarboxylating organisms, might we not think of the tubercle as a ductless gland, also turning into the blood stream some of these decarboxylated amino acids? The idea has received some attention, especially with reference to the production of histamine. I have proved that the tubercle bacillus is able to use histidine as its sole source of nitrogen, and Drs. Koessler and Hanke by their new methods have shown that histamine is not produced from histidine present in the medium, but that one of the corresponding deaminized organic acids, imidazolpropionic, pyruvic or lactic acid, is. These are innocuous substances.

The third possibility I had in mind to account for the alkaline tide is the withdrawal of phosphoric acid from the neutral phosphates present, for the construction of nucleoproteins and phospholipins, leaving the bases behind. I am convinced that this process plays some rôle, although it is probably small in comparison with possibility number one, which I outlined a moment ago, ammonia production.

Before leaving the subject of the Theobald Smith curve I should like to describe a simple method of following it, which saves time, and an immense amount of incubator space, obviating the necessity for the large number of cultures used where titrations are carried out each week. The method is not new, a similar one having been first used by Frothingham. I carry out the procedure as follows: A plaque of tubercle bacilli, approximately 1 cm. in diameter, less if necessary, is planted on 10 cc. of broth in a test tube, 1 inch in diameter, the broth being exactly neutral in reaction at the start, being either glycerol-peptone broth or a special medium, and containing 0.001 per cent of phenol-sulphonephthalein, which passes through a characteristic series of color changes between the hydrogen ion concentrations pH 6.4 and 8.4. At weekly intervals the tubes—I run the experiment in quadruplicate—are compared with standards containing the same concentration of indicator at different reactions, and the reaction curve is plotted. When 10 cc. amounts are used in well sealed tubes the whole procedure takes about two months. Obviously, it is much simpler than the titration method. This work is not quite ready for publication, but I may say that for H37 and B1 on glycerol broth, respectively human and bovine type strains from the Saranac Laboratory, I have secured curves quite comparable to those usually obtained by titration methods. The results on media of known composition are not yet as characteristic as I had hoped; and yet I believe that it is only by the use of such media that we shall ever be able to interpret the phenomenon. With certain saprophytes, such as smegma and grass bacilli, where glycerol need not be added, where a single amino acid, such as alanine, or acid amide, as propionamide, suffices for both carbon and nitrogen, striking results have already been obtained, which will be published in the near future.[2] They furnish very clear indications as to the protein metabolism of these organisms.

Inasmuch as the amino acid alanine can be considered as a type form for many members of the group, the ring compounds tyrosine, phenyl alanine, tryptophane and histidine, being simply substitution products of it, I am concentrating my attention on the products obtained from it, being at the present time engaged in the analysis of 2 litres of an alanine mixture upon which H37 was grown for one month. I am hoping to detect either ammonium lactate or ammonium pyruvate, ammonium propionate and ethyl amine, the other two possible decomposition forms, having been apparently ruled out.

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[2] See this number, p. 715.

In the investigation on metabolism up to the present time, I have run perhaps five thousand cultures of acid-fast organisms on media of known composition. Little of this has been published, as I confess that so far I have only accumulated many details without being able to establish broad general principles with which the details may be correlated. Bacteria, while chemical reagents, are very complicated reagents, not always of standard purity, so that many times the expected reaction does not take place and is replaced by another. Even so, I believe them more reliable reagents in our work than the higher forms of life, such as guinea pigs.

A brief summary of the details which have been observed should include the following facts. In general I have found, using human, bovine, and avian tubercle bacilli, frog, turtle and fish bacilli, leprosy bacilli, smega bacilli, and several strains of grass and mist bacilli, that nitrogen is readily abstracted from the amino acids alanine, leucine and histidine, and used successfully as the sole source of nitrogen. One conspicuous exception lies in the inability of my two avian strains to utilize alanine; they deaminize leucine readily however. The tubercle bacillus is able to thrive with alanine, leucine and histidine as sources of nitrogen, but not with tryptophane or phenylalanine. It might be thought that deaminization of these compounds did occur, but that growth did not proceed because the resultant product was toxic. As you know, one theory accounts for the stoppage of bacterial growth in old cultures on the ground that a high concentration of toxic products has been reached, for example from the tyrosine of the medium, which is nothing more than alanine with one hydrogen atom replaced by a molecule of carbolic acid, or from phenyl alanine where the replacement is with benzene. However, such reasoning cannot explain the failure of the tubercle bacillus to grow when phenyl alanine is supplied as the sole source of nitrogen, for when alanine is supplied in addition growth does occur.

As regards the utilization of the carbon in amino acids for structural purposes, it may be said that tubercle bacilli are unable to synthesize all the carbonaceous portion of their body substance from the material left after the abstraction of nitrogen. They need something else, best glycerol. Leprosy bacilli can slowly build up their organic body substance, all of it, from alanine or leucine. Frog, fish and turtle bacilli do the same thing a little better, but seem unable in general to split the ring compounds, such as tyrosine, tryptophane and histidine. The same statement may be made of the various grass bacilli, except that they do seem to split the imidazol ring of histidine. I am in this case, of course, taking it for granted that growth on histidine, as sole source of both carbon and nitrogen, means a splitting of the ring, as, naturally, proteins cannot be built up simply from piled up histidine molecules, and we have no evidence that bacteria take the straight chain for structural purposes—I grant they may oxidize it off—and throw the ring away. No organism of the group seems able to utilize tryptophane or tyrosine as sole source of both nitrogen and carbon. Inasmuch as some of the saprophytic acid-fasts are able to thrive on tryptophane and phenyl alanine, when glycerol is supplied as an additional source of carbon, I assume that the failure to grow on the ring compounds without glycerol indicates the inability of the organisms to split the indol and benzene rings.

As regards the utilization of nitrogen in other forms, I have found that propionamide is readily deaminized by all organisms of the group, that ammonia is a sufficient source of nitrogen for all members of the group, that creatinine, which contains imino, but not amino nitrogen, is used for nitrogen fairly readily by smegma and grass bacilli, somewhat sparingly by frog, fish and turtle bacilli, less readily still by leprosy bacilli, and by tubercle bacilli, as far as I can detect, not at all. Urea, which may be thought of as an amino acid amide, is used readily by all forms except tubercle bacilli, and turtle and fish bacilli. The ready use by leprosy bacilli is noteworthy.

No study of nutrition nowadays would be complete without a consideration of vitamines. They have been described as favorable to the growth of a variety of bacteria by several investigators. To be brief, I have not been able to demonstrate any growth increase with tubercle bacilli or other acid-fast organisms following the addition of certain market preparations of water-soluble (yeast) vitamine, or at least any increase which could not be attributed to the presence of certain useful amino acids, any increase which could not be duplicated by the addition of an "aminoid" mixture in which no vitamine constituency was supposed to be present at all. On the other hand, I have been able to prove that certain amino acids are useful *per se.* You are doubtless familiar with the work of Osborne and Mendel and others, who have shown that in mammalian metabolism lysine and tryptophane are necessary for growth and maintenance. I have been able to show that lysine, while not necessary to the growth of the tubercle bacillus, is at least desirable, for when you take two proteins, otherwise fairly similar, the one, edestin, containing lysine, the other, gliadin, being practically lacking in this substance, and prepare peptones from these and grow the tubercle bacillus upon them, you will find that the better growth occurs on edestin, the one with the amino acid lysine.

In conclusion, let me recapitulate the problems that I am considering, the study of which is being facilitated by a grant from this association. First, there is the type of nucleic acid present: what are its pyrimidine bases and what is its carbohydrate? Second, what sorts of protein are present in the tubercle bacillus? Then there is the subject of metabolism. How is phosphorus used? In the nitrogen metabolism how are amino acids broken up and what is the bearing of this breakdown on the reaction change of the medium? What happens to the cyclic amino acids, those substances from which physiologically active compounds are produced so readily? And lastly, a problem I have not yet touched: what is the rôle of glycerol in synthesis? This is a large order, and yet it touches but a few of the problems we must clear up for a moderately complete knowledge of the life history of the tubercle bacillus.

A METHOD OF FOLLOWING REACTION CHANGES IN CULTURES OF ACID-FAST BACTERIA

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In that graphic expression of acid and alkaline changes taking place in the culture media of tubercle bacilli which has for years been designated as the Theobald Smith curve (1), we are furnished with highly suggestive leads on the metabolism of this organism. From a protein-glycerol mixture both alkali and acid are produced at rates more or less constant for a given strain. The chemistry of the change has not yet been definitely worked out.

As orginally developed, the method of preparing the curve required large numbers of duplicate culture flasks, two or more of which would be taken for titration each week and then discarded. About four months were required for the complete cycle. The method was thus long and tedious, and required a large amount of incubator space for a single determination. This was before the days of ready determination of reaction by estimation of hydrogen ion concentration

A few years ago Frothingham (2) followed the reaction change in a culture of a human type bacillus, H37 of the Saranac Laboratory, using the potentiometer, and obtained a curve comparable to the one usually obtained by the old titration method, with a range of reaction which may be calculated from his figures as pH 8.15 to 5.52. A little later, the same author (3) studied the growth of tubercle bacilli on media to which small amounts of indicator had been added. Using brom-cresol-purple, he found that glycerol broth culture media of human type bacilli tended to become acid, while those of the bovine type remained alkaline. He concluded that brom-cresol-purple and litmus may be useful in determining H ion concentrations of culture media of tubercle bacilli and in distinguishing human and bovine types.

Recently Dernby (4) determined the limits of growth of a strain of tubercle bacillus (horse) as pH 6.0 and 7.6, and the optimum concentration for growth, pH 6.8 to 7.2. One of us (5) noted initial growth between pH 6.4 and 7.8 for a human type bacillus with no apparent inhibition at 5.4 or 7.8. It is thus able to carry on its biological activities through a fairly wide range of reaction.

We submit, herewith, a method similar to the one used by Frothingham, in which the change in reaction can be followed with a high degree of accuracy between the limits pH 6.4 and 8.4, using phenolsulphone-phthalein, which passes through a characteristic series of color change within those limits, as indicator. Four test tubes 1 inch wide, each containing 10 cc. of glycerol-peptone broth or any other liquid medium, neutral in reaction (pH 7.0), plus 0.001 per cent phenolsulphone-phthalein, are inoculated with plaques of tubercle bacilli, approximately 0.75 cm. in diameter, sealed with tin foil, and incubated at 37.5°C. Once a week the tubes are taken out and the color compared with standards of known reaction containing the same concentration of indicator. We use the Dernby and Avery (6) comparator, placing a tube of broth back of the standard when we are determining broth reactions, to compensate for the color of the medium. Apparently, at this concentration the indicator does not inhibit the growth of these organisms. Care must of course be taken that the plaque remains floating. The reactions of the four tubes are averaged in plotting the curve.

In developing the method, we have carried out a large number of determinations on rapidly growing saprophytic acid-fast organisms as well as tubercle bacilli, and have grown these organisms on culture media containing a single amino acid or acid amide as the sole source of both carbon and nitrogen, from which they must build the entire amount of their proteins, lipoids and carbohydrates. We have thus obtained considerable light on the metabolism of this group. A series of our reaction curves is given in twelve appended charts. The saprophytes were cultivated for about one week and tubercle bacilli for two months. By the method it is aimed to save time, trouble and the necessity of running large numbers of bulky cultures for a single curve.

Three strains of tubercle bacilli and two strains of grass bacilli and one of smegma bacillus were studied. One of the grass bacillus strains is called "timothy bacillus" because it has for years gone under that name in the Saranac Laboratory stock, to which it was originally supplied by Moeller. It differs from the other one in its reaction curve, as is seen from the figures, and also in that it is decidedly chromogenic. H37, and B1 are old, but virulent, cultures of human and bovine type tubercle bacilli. H104 is a highly virulent human type tubercle bacillus isolated from sputum in June, 1920. As will be noted, the initial reaction varies a little; in all cases the intention was to start the experiment at pH 7.0, but occasionally autoclaving changed the reaction slightly, and the experiment was proceeded with at the new reaction.

SUMMARY OF RESULTS

Saprophytes: On glycerol-peptone broth the grass bacillus caused a slight acidity, the timothy bacillus a distinct alkalinity, and the smegma bacillus little change, in spite of good growth. On alanine the grass bacillus caused a distinct acidity, the timothy bacillus a distinct alkalinity, and the smegma bacillus little change. It will be noted that the results for glycerol-peptone broth and alanine are about the same. This is to be expected, in view of the fact that peptone consists almost entirely of polymerized amino acids like alanine: the same reaction change would result in both from a given cause. The glycerol, highly necessary as it is for tubercle bacilli, probably plays little part here, as these organisms thrive on peptone alone. On propionamide, which differs from alanine in the location of its amino group, all organisms caused a marked alkalinity.

Tubercle bacilli: H37 on glycerol broth gave the curve generally considered to be characteristic of human type bacillus, a primary alkalinity followed by a progressive acidity. It is to be noted that the change in reaction occurred much sooner than is the case in the flask titration method. This is presumably due to the small volume used, 10 cc., which would respond quickly to the elaboration of small amounts of acid and alkali. We feel that this rapidity is a distinct advantage of the method. B1 also gave the curve said to be characteristic for the bovine type bacillus, an initially increasing alkalinity, which later decreased, but not to the point of neutrality. H104 culture became alkaline and remained so for two months. No change was to be noted in any of these cultures after that time. The curve of H104 was thus not of the classic human type. It is simply one of the numerous exceptions.

The chemistry of these changes will not be gone into at the present time, as this paper is of the nature of a preliminary report on method. We are concerned now with simplifying old methods and establishing that characteristic curves can be secured on simple media of known composition with some organisms. So far, characteristic results for tubercle bacilli on simple media have not been secured. Our problem is to modify such media enough to promote good growth and yet not enough to complicate chemical interpretation. It is the chemistry of the change which we wish to understand, for its bearing on the organism's metabolism.

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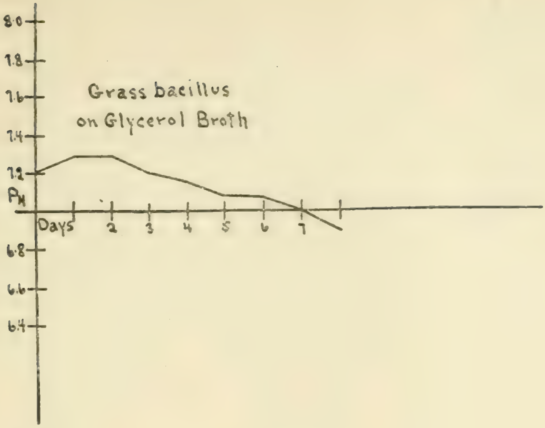
Grass bacillus
on Glycerol Broth
8.0
7.8
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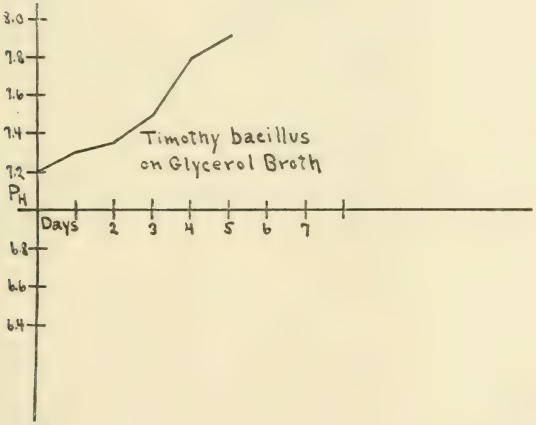
8.0
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Timothy bacillus
on Glycerol Broth
7.2
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Days
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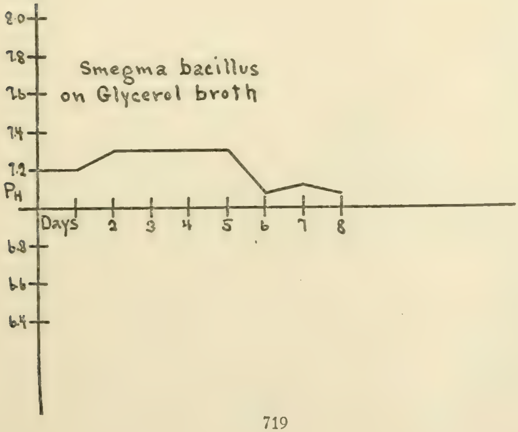
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Smegma bacillus
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on Glycerol broth
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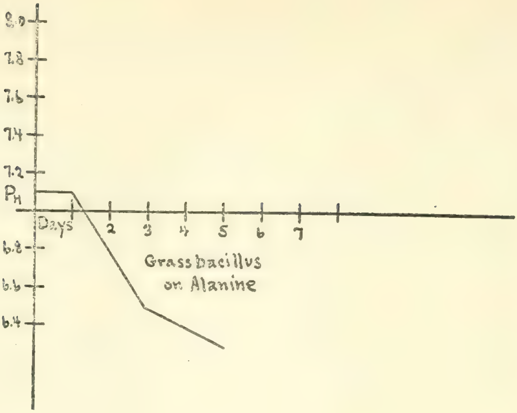
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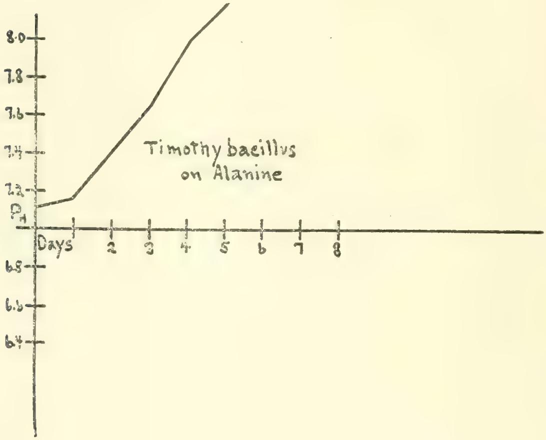
Grass bacillus
on Alanine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Timothy bacillus
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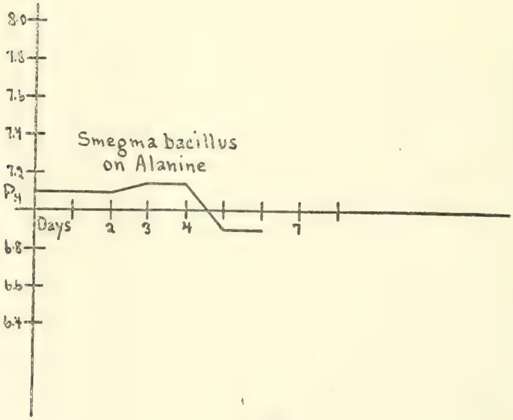
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Smegma bacillus
on Alanine
Days
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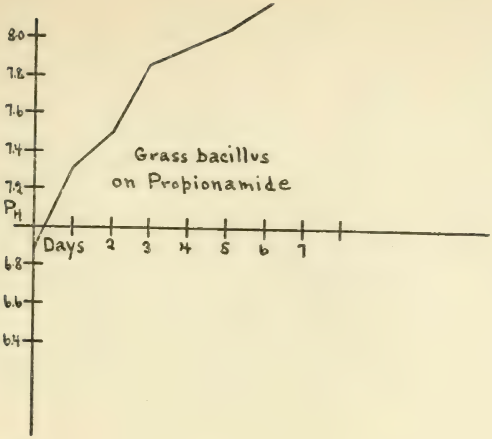
Grass bacillus
on Propionamide
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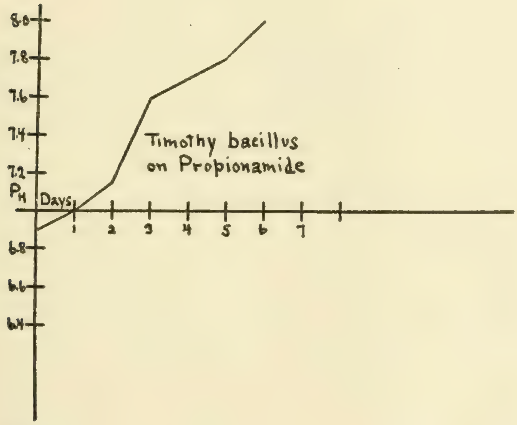
Timothy bacillus
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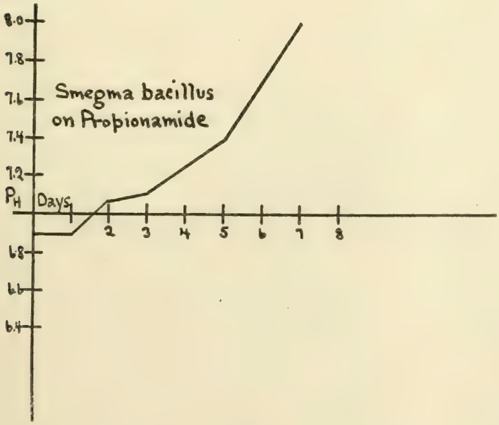
Smegma bacillus
on Propionamide
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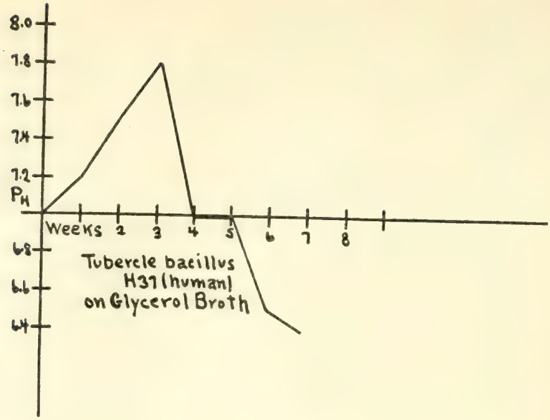
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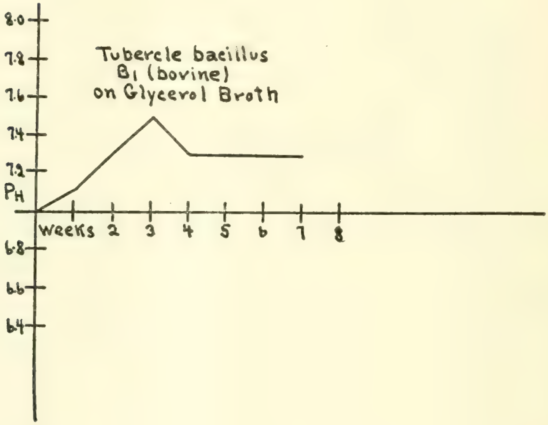
Tubercle bacillus
H37 (human)
on Glycerol Broth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Tubercle bacillus
B1 (bovine)
on Glycerol Broth
Weeks 2 3 4 5 6 7 8
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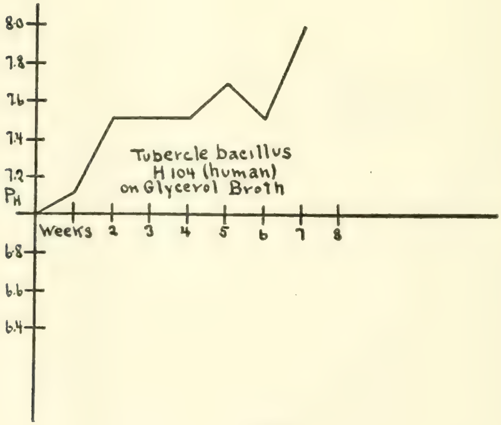
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ROENTGENOGRAPHIC PLEURAL ANNULAR SHADOWS IN PULMONARY TUBERCULOSIS[1]

AN INVESTIGATION OF THEIR CLINICAL SIGNIFICANCE AND A HYPOTHETICAL EXPLANATION OF THE MECHANISM OF THEIR FORMATION

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During the past five years, refinement of the standards of technique and interpretation in the roentgenographic study of tuberculosis has made possible a closer scrutiny of certain doubtful densities and, among other details, has directed attention to annular shadows. The formerly common error of interpreting all such shadows as parenchymal excavations is now generally recognized, and investigators have become engaged with the problem of determining the differential significance of these peculiar densities. The importance of their proper differentiation as influencing diagnostic accuracy, prognostic judgment and therapeutic indications is self-evident and has been emphasized in a number of creditable articles dealing with the distinguishing characteristics of genuine cavity and other annular shadows, situated in the planes of the pleural surfaces. That the last mentioned densities are the result of some inflammatory or mechanical alteration of the pleura is generally conceded, but beyond this a haze of disagreement beclouds understanding, largely because there are not sufficient autopsy data available to decide the issue and because no one has succeeded in reproducing the appearance in experimental animals. In lieu of this the only recourse has been to theorization based on roentgenographic and clinical observation. But one venturing into the unblazed wilderness of speculation is often prone to abandon or forget the compass of reason and, following the ignis fatuus of faulty premise, to arrive at a point which, to all appearances, is his proper destination but which, when projected with its environs on the map of previous knowledge, is found to be far afield. Such a tendency has been prominent in some of the attempts that have been made to explain pleural shadows with the result that a retracing of steps in search of bearings has become necessary.

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[1] Read in abstract before the Clinical Section at the Seventeenth Annual Meeting of the National Tuberculosis Association, June 15, 1921.

This communication aims to review the somewhat scanty literature on the subject, to supplement this with a clinical and roentgenographic investigation made at the Loomis Sanatorium, to criticize as untenable several theories that have been proposed, to reconcile accepted pathological and clinical facts with certain phases of the problem, to attempt to delineate in the light of present knowledge the zones of reason within which we may safely speculate, and to present a hypothesis to explain the formation, progress and disappearance of the shadows.

REVIEW OF THE LITERATURE

Sampson, Heise and Brown (1) performed a decidedly valuable service in being the first to call attention to the frequency of pleural annular shadows and to attempt an explanation of their purport. Their conclusions,[2] based on a careful and detailed study, were that pleural annular shadows "occur in patients more likely to be suffering from pulmonary softening and indicate rupture of the lung. Owing to the presence of adhesions, only partial pneumothorax with or without fluid results."

They found the condition in 11.8 per cent of 423 consecutive cases, in which it indicated a greater tendency to a recrudescence of the pulmonary disease. Of the 50 shadows studied, 60 per cent showed a transmission of the X-ray equal to that of the surrounding lung field and 70 per cent were located above the third rib, usually in one of the interlobar fissures. In a few of the shadows, the authors found horizontal fluid levels which they took to be small effusions in the presence of air. They reproduced experimentally *in vitro* an interlobar annular shadow the outer border of which was more sharply defined than the inner border. Evans (2) after observing the work of these authors arrived at similar conclusions, explaining the mode of formation of the shadows as follows: "First, there is a pleuritis with or without fluid, and then an ulceration or rupture of the lung tissue, so that air escapes into the area of pleuritis." The localized pneumothorax theory has apparently received general credence and Honeij (3) alone has registered himself as a dissenter, offering the explanation that

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[2] In a discussion at the Seventeenth Annual Meeting of the National Tuberculosis Association, Doctors Brown and Heise indicated that they had modified their views somewhat and were willing to consider a few of these shadows as due to simple pleurisies.

> Annular shadows are the result of adhesions between the parietal and parenchymal surfaces subsequent to inflammation. Under certain conditions there is an oval or circular arrangement of the pleura to the formation of which the movement of the lung and thorax contributes, resulting in the formation of a central or local pseudo-emphysema. The area around the annular shadow, which borders on the shadow, represents the more firmly attached or organized pleura.

Honeij holds further that these shadows "have no relation to pulmonary infiltration or softening and breaking down of tissue." The author does not outline the steps by which he arrived at his conclusions. Dunham and Hayes (4) have reported autopsies on two cases showing annular shadows. One of these proved to be "a large circular area of thickened attached pleura overlying a pyramid of caseation in the lung in which a cavity was found," and in the second case a cavity proved to be the underlying lesion.

ROENTGENOGRAPHIC AND CLINICAL STUDY

At the Loomis Sanatorium 50 annular shadows, occurring in 36 cases have been studied, and constitute the basis of the following report. A considerably larger number has been observed, but only those are here included that have been followed by detailed clinical records and two or more serial roentgenograms. It should be obvious that the determination of the true significance of the shadows necessitates a study both of their anatomical mutations and of contemporaneous variations in clinical symptoms. It is no more possible to acquire a clear conception of the phenomenon by single isolated pictures than it is to trace accurately changes in intrapulmonary tuberculosis without serial roentgenograms. Furthermore, it is felt that serial roentgenography eliminates as far as possible the error of confusing pleural shadows with cavities and, where there has been any reasonable doubt as to the correct interpretation, the case has not been included in the report. In 14 of the cases there were positive or doubtful physical signs of cavity; in 5 of these the signs were elicited in the opposite lung and in the 9 cases where the signs were homolateral the roentgenograms showed cavitation in addition to the pleural change. The nature of the pulmonary disease was conclusively proved by the presence of tubercle bacilli in the sputum in all cases.

To consider first the roentgenographic characteristics of annular shadows, it should be noted that many of them are not annular, but may appear as other more or less complete geometrical figures, such as semicircles and triangles. In this group of 50 shadows, 19 were circular, 21 were ovoid and 10 were irregular or incomplete. In almost all of the ovoid shadows the longer diameter lay in the horizontal plane of the chest (erect posture). The "rings" varied in appearance from a light, filmy cloud, resembling closely a ring of tobacco smoke as blown from the mouth, to a dense and compact figure, the border of which may be a narrow line or a wide homogeneous clouding spreading over a large portion of the lung field. The shadows may be multiple, and in one case there were three in one field and two in the other. The translucency of the centre of the shadow is a matter of importance. In 17 of this series of 50 shadows the area within the borders of the "ring" was greater in density than the surrounding pulmonary field; in 33 cases there was no detectable difference in density. In almost all instances unbroken lung markings could be made out beneath the translucent centre of the shadow. In no case was the annular shadow rarefied as compared with other lung markings. The comparative definition of the inner and outer borders of the shadows should be noted also, since this factor has some

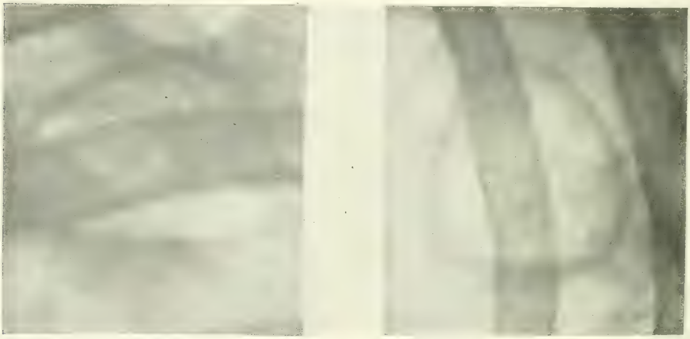
Fig. 1 Fig. 2

FIG. 1. PLEURAL ANNULAR SHADOW IN RIGHT CHEST SHOWING A HORIZONTAL FLUID LEVEL IN THE DEPENDENT PORTION

Patient sitting in erect posture (postero-anterior view)

FIG. 2. SAME SHADOW AS SHOWN IN FIGURE 1

Roentgenograms taken with patient lying on his left side. Note shifting of the fluid level with changes of posture. (Antero-posterior view.)

bearing on their proper explanation. In 39 or 78 per cent of this series the inner border was more sharply defined than the outer border; in 11 or 22 per cent the definition was equal and in no case was the outer border better defined than the inner.

In 13 of the series a horizontal line, suggesting fluid, was observed in the dependent portion. In 4 instances the presence of fluid was demonstrated by the shifting of the level with change of the patient's posture (figures 1 and 2). In 3 cases the level was proved to be an illusory phenomenon, depending on the degree of obliquity of the penetrating X-ray. In the remaining 6 shadows it was not possible to investigate the point. In one instance the horizontal line disappeared in the space of four days.

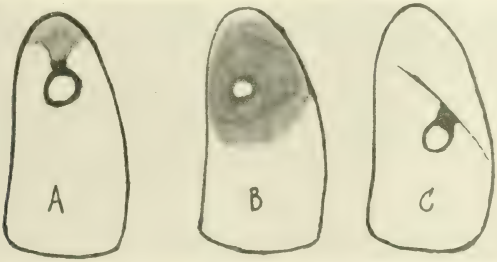

Diagram 1. To Show Character of Pleural Densities Adjacent to the Annular Shadows

At *A* this shows as a cap of thickened pleura extending from the annular shadow over the apex of the lung. At *B* there is an extensive area of pleural thickening spreading out in all directions. At *C* the upper border of the annular shadow merges with and is sharply defined by a band of interlobar pleurisy. (Sketched from X-ray negative.)

In a great many cases, more or less heavy striations were seen extending along the pleural surfaces to the annular shadow; these were taken to be thickened lymphatic trunks draining the area of inflammation. Most of them extended to the hilum; but in four instances where the shadows were situated in contact with the parietal pleura they extended to the mediastinum. In all cases where the shadow was located in the interlobar fissures, the trunks led to the hilum; an expected observation, if we remember that the lymphatics of the visceral pleura drain toward the tracheobronchial nodes. In several cases there were other contiguous pleural shadows of rather unusual appearance (diagram 1). These were always in the form of localized pleural thickenings, shading off from the outer border of the annular shadow; in two cases this border was sharply cut by bands of interlobar pachypleuritis.

The location of the shadows is also of moment. This series of 50 was distributed in the following way: 4 lay in contact with the anterior chest wall between the second and fourth ribs; 23 were situated posteriorly, 1 above the level of the third rib, 7 entirely above the sixth rib, 14 above the eighth and 1 above the ninth rib. Twenty-three lay in the planes of the interlobar fissures, 3 above the level of the body of the fourth thoracic vertebra, 18 above the seventh and 2 above the eighth. It is possible that a few of those visualized close to the posterior chest wall really lay in one of the pleural fissures; but the point to be emphasized here is that 46 of the shadows were located either in the fissures or in contact with the posterior parietal pleura and a vast majority of them were in the upper half of the chest. Twenty-seven of the shadows were in the right chest and 23 in the left.

At the beginning of the work it was anticipated that an investigation of the mutations of pleural annular shadows by serial roentgenograms would shed some light on the problem of determining their significance; and it may be fairly said that such a study of this series has amply fulfilled expectations. Twenty of the 50 shadows increased in size. This increase was brought about by an extension of the circumference of the shadow, usually equally in all directions. Thus, a ring that measured 4 cm. in diameter two months ago might have an appearance generally identical except that it measures 6 cm. in diameter to-day. Except for the changed dimensions there is nothing to indicate the alteration, the area within the ring having a homogenous translucency. One shadow has been observed from its very incipiency; this started as a cottony, poorly defined cloud, and later the centre of the cloud cleared, leaving a peripheral annular density. The ring disappeared, but eventually reappeared and became larger. The point to be raised here is whether this did not represent the excavation of a small caseous area within the lung, a point for which no positive proof can be offered, but the area behaved in a way that is characteristic of annular shadows, as opposed to the changes typically observed in cavities: there was no discernible rarefaction; it looked precisely like other pleural shadows developing in the same case and impartial judgment was in favor of a a pleural process. In two cases, where the shadows entirely faded and later reappeared, the size of the second appearance was greater than the maximum size of the first one. As annular shadows develop and enlarge they may actually overlie areas of rarefaction definitely representing cavitation; in such cases the differential diagnosis is often rendered easier by the contrast.

In 16 instances the shadows decreased in size and in 12 they entirely disappeared. These changes were accomplished by a concentric decrease in the circumference of the ring, but it was observed that the ring never shrank to a point where it lost its annular character. Thus, if a ring disappeared, it first decreased its diameter and circumference; then the size remained stationary and there was a gradual fading of the density of the circumference, until it could no longer be distinguished from the surrounding markings, or until all that remained was usually a faint amorphous clouding. In two cases the rings were finally replaced by plaques of pleural thickening. These plaques, under the stereoscope, were noted to be in exactly the same location as the preceding annular shadows; they appeared as thin leaves of a homogeneous density and with their peripheries clearly and sharply cut. One of these cases is illustrated (figures 3 and 4), showing the localized plaque of pleural thickening persisting at the site of the annular shadow after an interval of six years.

An intimate knowledge of the clinical course of the 36 patients in whom these 50 shadows have been studied has been of utmost use; and a correlation of this knowledge with the anatomical mutations observed has resulted in the evolution of certain laws that practically invariably apply to the various phases of development of all the shadows. In all cases in which annular shadows developed there were positive symptoms of active pulmonary tuberculosis immediately or closely preceding the detection of the pleural process; in every instance such symptoms were evident within a month previous to the first discovery of the shadow. Conversely, an annular shadow has never been seen to appear where there was definite clinical or roentgenographic evidence of retrogressive disease. In 19 of the 20 instances in which the annular shadows increased in size, there were definite clinical or roentgenographic signs of active and progressive pulmonary disease; in one case there were no apparent changes in the lung lesion, but the period of observation was short (six weeks). A shadow was never seen to become larger where there was demonstrable evidence that the pulmonary lesion was quiescent or retrogressive. Of the 28 instances where the shadows decreased in size or entirely disappeared, the pulmonary disease was definitely retrogressive in 27 and stationary in 1; in no case did a shadow become smaller or disappear if there was evidence of active and progressive pulmonary tuberculosis. In two instances the size of the rings did not change and the pulmonary condition remained stationary.

In 3 cases in which the rings disappeared artificial pneumothorax had previously been induced on the same side. In two of these the annular

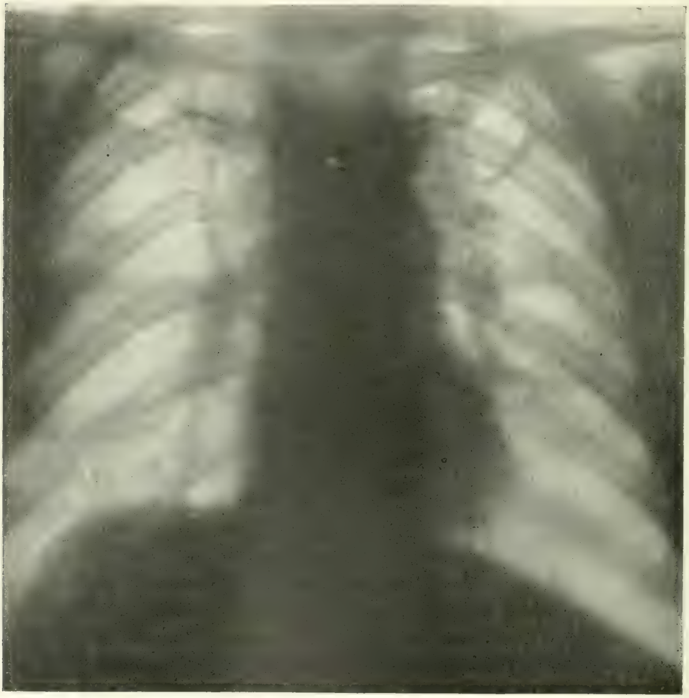

Fig. 3. Roentgenogram Shows on the Left Side a Semicircle in Front of the Fourth and Fifth Ribs Posteriorly and a Completely Formed Annular Shadow in Front of the Sixth and Seventh Interspaces Posteriorly

In the stereogram these shadows have all the characteristics of pleural densities and lower one does not merge with the hilum as the figure would indicate. This picture was taken July 13, 1913. No physical or clinical evidence of cavity.

shadows were in contact with the posterior thoracic wall and, following collapse of the lung, adhesions could be made out between the visceral and parietal pleurae at and about the site of the former ring. In the other case the ring was in the interlobar fissure and, after being collapsed for seventeen months, the lung was allowed to reëxpand, showing no trace of the shadow.

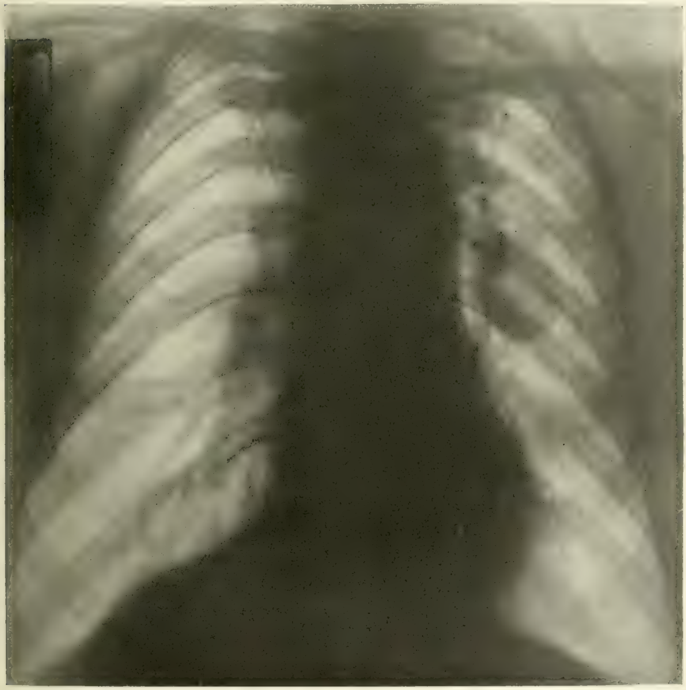

Fig. 4. Same Patient as Figure 3. Roentgenogram Made after an Interval of Six Years (September 4, 1919).

Note that the upper semicircle has entirely disappeared and the disc-like density that has replaced the lower annular shadow. In the stereogram this density appears as a plaque of thickened pleura sharply defined above by a thin line of interlobar thickening. Note the hilum showing through the translucent area of residual pleural thickening. Patient is well and has had no symptoms of tuberculosis for five years; physical signs of a healed lesion.

In 6 cases the annular shadows showed combinations of changes, increasing in size first and then decreasing, or vice versa. It was striking to see how closely these changes followed the course of the pulmonary disease and two cases may be cited as examples. In one the annular shadow decreased in size and then, in a few months, became larger; several weeks later a pleural effusion developed on the opposite side. In the second case the patient's favorable course was interrupted by an hemoptysis and subsequent febrile reaction; roentgenograms showed that a previously diminishing annular shadow had reversed its course and grown larger. These cases are typical.

A word should be said about the criteria of active and retrogressive disease here employed. A lesion was not considered active unless there were definite manifestations of toxemia, such as fever and tachycardia, or actual roentgenographic evidence of an extension of the tuberculous process; in almost all cases the evidence was both clinical and roentgenographic. As might be expected, a certain number of patients previous to the discovery of the annular shadow and previous to their admission to the sanatorium, were ambulant. Disease was not considered retrogressive until there was definite abatement of the constitutional symptoms and roentgenographic evidence of reparative changes in the lesion.

No special effort was made to determine the rate of incidence of annular shadows; but estimates have been made from time to time and this rate has been found to be as high as 20 per cent. Thus, in one series of 100 consecutive admissions to the sanatorium, the shadows were seen in 20 cases.

In no case were there any typical symptoms or signs to indicate pleural rupture and subsequent pneumothorax. None of the patients complained of a sudden stabbing chest pain or sudden shortness of breath or sudden onset of paroxysmal coughing. None were cyanotic, nor were any physical signs of pneumothorax elicited. It is not to be inferred from this that we have failed to consider cases of typical localized pneumothorax and those atypical cases variouly described as "silent pneumothorax," "latent pneumothorax," or "*pneumothorax muet;*" but such cases have not been frequent in our experience and have not been, included in this study. Indeed, we have found but one constant clinical feature accompanying the appearance of annular shadows; this has been, as mentioned above, that the patients always manifested clinical or roentgenographic evidence of active and progressive pulmonary tuberculosis. In many of the cases there were chest pains, but these were of the vague, dull, aching and more or less constant character, complained of at some time by almost every patient with pulmonary involvement. In 14 cases there were frank hemoptyses and in 10 streaked sputum; such a rate of incidence is to be expected in active disease. Fever was a common symptom and in one case it followed an unusual course. This patient had a temperature curve that presented the appearance of a series of waves, each wave extending over a week or two with its crest at 102° or 103° (rectal) and its trough at or near the normal line. A roentgenogram, taken after one or two of these waves had passed, always showed the enlargement of previously existing rings or the development of new ones, until, at the end of seven months, five separate rings could be distinguished. Similar changes were noted less strikingly in other cases.

The rate of change in the size of annular shadows varied, and seemed to be related to the degree of activity and progression or retrogression of the pulmonary disease. In the case just cited, the rings enlarged and multiplied with comparatively great rapidity. In disease that is markedly active and accompanied by persistent or undulating fever, tachycardia, and other signs of profound toxemia, an annular shadow may form in the space of several weeks. Between this and stationary disease, where the shadow may remain *in statu quo*, there are all gradations of change to be expected; for instance, a shadow has been seen to require eight months to lengthen its diameter by one centimetre. The patient's course was that of slowly progressive, chronic disease with occasional slight elevation of temperature and rapid pulse. A diminution in the size of the shadow is slower; this is to be expected, since retrogressive and reparative changes in the pulmonary lesion are usually more gradual than progressive and destructive mutations. In one patient whose disease showed progressive improvement, the vestige of his annular shadow could be traced in roentgenograms two years from its first detection. Small shadows may disappear in a month but, on the average, from four months to a year or more are required. Residual pleural thickening may last indefinitely; in the one case mentioned (figures 3 and 4) it was observed after six years. Fluid, when present, may disappear within a week after the disease becomes retrogressive.

CONSIDERATION OF PRESENT THEORIES

The study has led to the belief that these annular shadows cannot be explained by the lung rupture theory of Sampson, Heise and Brown; on the contrary, it seems that the vast majority of them must and can be explained on other grounds. Before considering the detailed reasons for the latter statement, the evidence that tends to nullify the lung rupture theory will be presented.

Clinical and pathological experience would indicate that the rate of incidence of spontaneous rupture is not as high as that of pleural annular shadows. The authors referred to found such shadows in 11.8 per cent of 423 consecutive cases; our experience, though not conclusive, suggests that the figure may go as high as 20 per cent. Remembering that the phenomenon was found to appear only in patients manifesting clinically active or progressive pulmonary disease, it should be expected that in this particular group the incidence would be considerably higher. In fact, the investigation has engendered the conviction that, if every case of pulmonary tuberculosis were radiographed at frequent intervals during the period of progression and destruction, these shadows would appear with astonishing frequency. To such figures must be added those cases of frank and easily recognizable pleural rupture followed by massive lung collapse. In contrast to such a large total, clinical and autopsy figures indicate that the rate of incidence of spontaneous pneumothorax in pulmonary tuberculosis, including those cases with fatal issue, does not exceed 10 per cent; more conservative writers put the figure at from 5 to 6 per cent. West (5) found the rate to be 5 per cent in 1175 cases, and gathered from the literature 1878 cases in which it was 3.4 per cent. Babcock (6) gives as his figures from 1 to 6.5 per cent. At the Brompton Hospital (7) the incidence was 8.2 per cent among 1069 autopsies from 1887 to 1894, and 6.4 per cent in 263 autopsies from 1900 to 1903. Powell and Hartley (7) believe that about 6 per cent of all cases of phthisis die with pneumothorax. Stanton (8) found 25 cases in 337 autopsies, or 7.32 per cent, at the Phipps Institute, and quotes Weil's findings of 10.1 per cent in 355 autopsies. Many papers on this phase of the subject confuse the mortality rate with the general incidence among living cases, whereas, in the latter group the frequency is much lower. Thus Fussell and Riesman (quoted by Babcock) found a rate of less than one per cent in 58,731 cases. West quotes Biach's figure of 1 per cent, but thinks this is too high. Landis (9) says pneumothorax may be expected as a complication of pulmonary tuberculosis in 5 per cent of all cases. Dunham (10), by X-ray studies, found it in 1.5 per cent of 2000 cases admitted to the U. S. A. General Hospital No. 19 at Asheville. It is readily seen that the rate of incidence of pleural annular shadows exceeds the highest of the figures cited, evidence that does not speak very eloquently for the lung rupture theory. Barlow and Thompson (11) hold that small localized pneumothorax is the rule rather than the exception in pulmonary tuberculosis; and explain that it usually disappears before death and, even if persistent, would be destroyed in the separation of the lung from the thoracic wall. This contention is almost incredible and the details of their investigation, to be published later as a monograph, will be awaited with interest. It is true that the pneumothorax pocket may be destroyed in the course of the autopsy, but it seems only reasonable that a fairly large percentage of the pleural perforations should be detected by the pathologist. Just why the condition should usually disappear before death is difficult to see since, in the figures quoted above, rupture of the pleura is shown to be many times more frequent as a terminal event than as a general accident.

Sampson, Heise and Brown found most of their shadows above the third rib and usually in one of the interlobar fissures. In the series reported here, 46 of the 50 cases were situated posteriorly, above the level of the eighth thoracic vertebra or in the upper part of one of the interlobar fissures. The theory of the Trudeau investigators is contingent on the assumption that pleuritis must exist before the lung ruptures, and predicates that rupture occurs into an area completely shut off from the remainder of the pleural cavity by adhesions. It therefore follows that the pleural perforation must be located within the area of the annular shadow. It is true that adhesions are often found in the regions where annular shadows most frequently appear, but it is strikingly and equally true that perforations are not usually discovered there. Witness the statement of Louis (12) to the contrary: "The perforation occurred in five-sixths of the cases near the angles of the third or fourth ribs; that is, in a place corresponding to that where the pain was felt and where pleuritic adhesions, when not general, commonly terminate." In Stanton's series of 15 cases, where the perforation was found, the rupture was in the upper lobe in 12, lower lobe in 2, and between the upper and lower lobes in one. The last case, by virtue of its standing conspicuously alone, emphasizes the fact that few perforations occur in the interlobar pleurae, a fact in forceful contrast to the very frequent occurrence of annular shadows in these fissures. Adhesions are most frequently found in the interlobes; and this again is the reason perforation is so unusual in these localities. Landis (9) finds that the lung rupture occurs most often "in the lateral portion of the upper lobe between the third and sixth ribs." Powell and Hartley (7) apparently agree to this, giving the location as "usually found in the upper half of the lung, though rarely higher than the third rib, since above this point the pleural cavity is generally obliterated by adhesions." To these may be added the observation of West (5) that

> the favorite position of the opening is in the postero-lateral region, in the lower part of the upper third of the lung, and, therefore, usually in the lower part of the upper lobe. This is, no doubt, to be explained by the fact that in most cases the upper part of the pleural cavity is obliterated by adhesions and that perforation takes place immediately below them.

Following the pleural rupture the resulting pneumothorax, if it is only partial, is usually confined to the lower half of the chest; this observation is so common that it may be taken for granted without argument.

These bits of evidence may, therefore, be summed up as follows: Where annular shadows appear most often, pleural perforations are not commonly found at autopsy; likewise, the resulting partial collapse of the lung is usually confined to the lower half of the chest, whereas annular shadows, presumed by Sampson, Heise and Brown to represent air pockets, are almost always seen in the upper half. Such discrepancies do not find ready explanation and cast the shadow of doubt on the validity of the lung rupture theory.

Pleural annular shadows do not bear the hallmark of typical partial pneumothorax. The points of differential roentgenographic diagnosis of such air pockets are fairly stated by Steiner (13) as follows: Absence of linear tracings; usually at bases; rarely at apex; outline of lung and visceral pleura usually shows; usually irregular; never rounded or circular; bands or strings of pleural adhesions can often be seen. Annular shadows do not present one of these characteristics; and this evidence alone throws a burden of proof on those who would adhere to the pneumothorax theory. But even granting that these shadows may be notable exceptions to the rule, it remains for the proponents of the theory to explain the mutations observed. The shrinkage of the shadows may be considered as in accord with the gradual diminution in the size of pleural air pockets, but the mechanism of the enlargement of the shadows cannot be elucidated with such facility. True, with pneumothorax artifically induced, adhesions can be stretched and the space made larger but this is accomplished by persistent and multiple refills and positive pressure. It cannot be conceived, in the light of the theory proposed, how the assumed air pocket, enclosed by adhesions as represented by the annular cloud, is to be kept filled with air under pressure sufficient to stretch the adhesions and allow the enlargement of the space. To cite a specific instance, the series reported above contains several annular shadows that doubled their diameter in a space of three to six months. The only explanation that could be given on this theory is that there were valvular perforations which remained patent and allowed air to escape into the pocket throughout these months under such pressure as to forcibly stretch the adhesions. The improbability of this is so great that it scarcely needs mentioning. Indeed, it is the common experience of those who have used artificial pneumothorax that small air pockets, enclosed by adhesions, will become progressively smaller and finally obliterated in spite of all efforts to maintain the lung collapse.

Annular shadows may be multiple; but this factor does not afford much evidence, positive or negative, since pleural perforations may also be multiple. Louis (12) reported a case in which he found fifteen perforations. The point is that multiple pleural ruptures usually result in the death of the patient, whereas a patient with five of these annular shadows has survived for more than a year, with only those symptoms to be expected from an active pulmonary lesion.

In none of this series were there any acute symptoms to indicate lung rupture, nor were such symptoms mentioned by Sampson, Heise and Brown. We know that "silent pneumothorax" is a true clinical occurrence but, heretofore, it has been considered uncommon, and the onset of lung rupture is usually marked by violent pain, and followed by dyspnea and possibly cyanosis, all of which are characterized by the suddenness of the accident. We may follow to some extent the reasoning of Louis (12) because it is just as sound now as it was in the earlier days of clinical investigation. After describing the train of events he says:

> These symptoms are so much in conformity with what might, under the circumstances, be anticipated that they appear almost as if determined *a priori;* and in consequence of the similitude of the conditions attending perforation of the small intestine and that of the lungs their nature might, further, it appears to me, have been suspected by reasoning on analogy. In one and

the other case in truth, effusion of an irritating liquid into a serous sac takes place at the moment of perforation; and as sudden pain and the various symptoms of acute and violent inflammation arise in the one case, they might be expected to declare themselves in the other. And again, as suddenly developed pain in a given spot in the abdomen, accompanied by the symptoms of intense peritonitis, suffices for the diagnosis of perforation of the intestine, it might fairly be supposed that the same would be the case in the instance of the lungs,—and the pain, similarly sudden and intense, in one side of the chest, combined with extreme dyspnea, and the other symptoms of pleurisy would suffice, more especially in phthisical subjects, to announce that the pleura has given away.

Such compelling logic cannot be circumvented. Only a desire that any error should be on the side of conservatism prevents the assertion that it is impossible that a hundred lung perforations (50 in the Trudeau series and 50 in this series) should occur without once precipitating the symptoms of perforation.

In the cases reported here, no signs of pneumothorax were elicited, a matter of no special significance, since small pleural air pockets often exist without recognizable signs. It was noticed that in certain cases râles of a superficial character increased at the site of the shadows.

All investigators agree that the spontaneous rupture of the lung generally results in an effusion into the pleural cavity. West (5) estimates that in two-thirds of the cases the effusion is seropurulent, and in the remaining third it is serous. A few annular shadows are known to contain fluid, and the number would probably be greater if it were possible to make observations at frequent intervals over long periods of time. But the effusions, when present, were not purulent, because there were never any typical symptoms of sepsis. By implication, if not by open avowal, the theory of Sampson, Heise and Brown is largely based on the fact that the fluid level in annular shadows shifts with a change in the patient's posture, a fact indicating to them that air, presumably escaped through the pleural opening, must also be present. This premise is false, because it is a well known physical phenomenon that fluid readily and quickly shifts in the presence of a vacuum or any degree of a partial vacuum. The classical water hammer experiment can be cited as proof. It is to be expected then that, if through any agency the pleural surfaces became separated and the intervening space became partly filled with fluid, the fluid would not only have an upper horizontal level but would also shift as the position of the containing sac was changed. Further on, evidence will be offered to indicate that just such conditions may exist and, if this evidence is convincing, then the mainstay of the pneumothorax theory collapses.

The mortality from spontaneous pleural rupture is estimated by Bandelier and Roepke (14) as 80 per cent. Thus far no mortalities have been reported as due to the condition represented by the annular shadow.

Sampson, Heise and Brown reproduced experimentally several annular shadows, but their outer borders were better defined than the inner borders. In this series, such a relationship was never seen; in 78 per cent the inner border was better defined, and in the remaining 22 per cent the definition of the inner and outer borders was equal.

These authors found that the presence of the annular shadow indicates a somewhat graver prognosis, presumably on account of the lung rupture and resulting pneumothorax, but it may be reasoned *a fortiori* that the outlook is less favorable, not because of the local phenomenon *per se*, but because of the active and progressive intrapulmonary lesion that, in our experience, has been an invariable accompaniment of the newly developing and enlarging annular shadow.

These, then, are the practical and theoretical considerations that seem to render the lung rupture theory untenable and constrain us to seek some other explanation for the existence of pleural annular shadows,—an explanation that should have the merit of probability. It may be true that there are a number of causes and, with this in mind, it must be granted that a few of the shadows may indicate "silent pneumothoraces," but these seem to be the exceptions to some rule that has not as yet been formulated. Barlow (15) thinks that in some cases the shadow produced by lung collapse lies, not in the pleura, but in the adjacent lung, which, if true, would render interpretation even more difficult. Probably some so called pleural shadows are really cavity shadows, but it is believed that this potential error is minimal in the series reported above.

Knowing the frequency of pleuritic processes, it is only natural that we should turn in this direction in search of some peculiar inflammatory change that would have a roentgenographic counterpart corresponding to the annular shadow. Honeij's (3) explanation is based on such a phenomenon; but it is difficult to follow his reasoning that the shadow is due to a local pseudo-emphysema resulting from "an oval or circular arrangement of the pleura." There are no available physiological facts to support this obscure explanation. He holds further that the shadows have no relation to pulmonary infiltration or softening and breaking down of tissue. The investigation at Loomis has not only disproved this, but has proved the fact to be directly opposite; namely, that this series of annular shadows developed and enlarged as an accompaniment of active intrapulmonary lesions. Our study points to simple localized pleurisy as the cause of the annular shadow, but the mechanism of its formation must be explained on more ratinal grounds. In the following paragraphs this hypothesis will be elaborated and the line of reasoning for its support will be outlined.

THE SIMPLE PLEURISY HYPOTHESIS

The rate of incidence of annular shadows is altogether compatible with that of localized pleurisies. "That the pleura is one of the battlefields in the great struggle between the invaded organism and the tubercle bacillus cannot be doubted in view of the damage done," is the opinion of C. Y. White (16), and he has sufficient support for his belief. Indeed, the frequency of pleural adhesions in pulmonary tuberculosis is one of its well known and conspicuous features, and no thesis need be proposed for its proof.

It has been shown that annular shadows are most frequently situated above the level of the seventh or eighth vertebral bodies, between the posterior parietal and visceral pleurae, or in the upper part of one of the interlobar fissures, and that these are the points at which lung rupture is uncommonly found. There is before us, then, a rather remarkable contrast when we recollect that these are the very sites at which pleuritic changes are most often found. Again referring to White (17), whose work was based on careful and extensive autopsy investigations at the Phipps Institute it is shown that "the partial or complete obliteration of the interlobar space by the adhesion of the pleural surfaces is rather the rule than the exception in chronic tuberculosis of the lungs." This, he continues, may be in the form of a fibrous tissue septum with or without typical tuberculous deposits, or of loose isolated bands of adhesions of varying length. Outside of the interlobes he (18) found lesions of the pleura (adhesions), generally posteriorly at the apex of the upper lobes or 2 or 5 cm. below the apex posteriorly, more frequently on the right than on the left, and on both sides more frequently posteriorly than anteriorly. It will be recalled that in the series herein reported only four annular shadows were seen in contact with the anterior chest wall, and these were between the second and fourth ribs. The number is very small, but they should be considered in the light of White's experience (18) that, besides the places above mentioned, "a favorite site seems to be along the course of the third, fourth and fifth ribs anteriorly from the parasternal or midclavicular line to the midaxillary line." They "usually appear as delicate bands following the course of the ribs." In considering the factor of location, therefore, a strikingly close correspondence between annular shadows and simple pleuritic changes is observed, so close that it must be reckoned with in any attempt to solve the main problem.

Turning to another point, it is generally agreed that the shadows represent some process that is by nature localized and, further, this study has shown that their development is an accompaniment of an advancing intrapulmonary lesion. These again are characteristic features of tuberculous pleurisy secondary to pulmonary involvement. That the pleural damage usually follows the advance of the pulmonary infiltration is commonly recognized. In the foregoing reference to White's work, it was noted that interlobar adhesions may be isolated. Elaborating on this point he says (17):

> As the term implies there are found throughout the pleural cavity, over one or more lobes, areas of old dense and of recent adhesions. The presence of the old and recent adhesions suggests the way the process becomes widespread. It is likely that the isolated adhesions found at autopsy represent repeated injuries to the pleura from localized conditions in the lungs. In these cases, even when the adhesions are distributed throughout almost the whole pleura, small areas of practically normal pleura are to be found.

The coincidence of these important peculiarities of annular shadows in the roentgenogram and of localized pleurisies in the pathological picture aids materially in building a chain of evidence in favor of the localized pleurisy hypothesis. What other pleural process, we may ask, having the two outstanding characteristics mentioned in this paragraph, occurs with equal frequency in pulmonary tuberculosis? This challenge, it is believed, must stand without an adequate answer.

The clinical symptoms accompanying the development of annular shadows do not eliminate pleurisy as a possible contributing cause. This evidence is largely of a negative character; but it is valuable as such, because pleural inflammatory changes may occur with no characteristic manifestations save the symptoms that commonly mark an actively advancing pulmonary lesion.

The roentgenographic appearances furnish evidence of a more positive purport. Localized pleurisies persist indefinitely and may leave permanent changes, thus affording a possible explanation for the fact that vestiges of annular shadows may be discerned for as long as two years and more. It would also be expected, therefore, that any permanent residuum of the annular shadow would be of the nature of pleural thickening, and this has been shown to be true in a number of the series. That there are localized adhesions at the site of the annular shadows has been shown by Evans (2) and also here by the roentgenogram following the induction of artificial pneumothorax. It is also to be remembered that one of the two cases of Dunham and Hayes (4) showed at autopsy "a large circular area of thickened attached pleura." It is true that this covered a pyramid of caseation containing a cavity, but it has been shown that such lesions may be recognized in combination in the roentgenogram; and it is just such a localized patch of pleurisy that may cause, as will be explained further, the annular density in the roentgenogram.

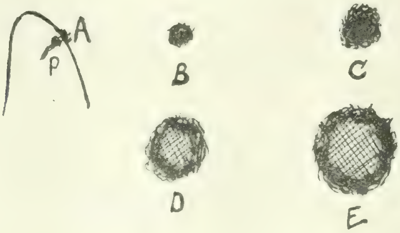

Diagram 2. Illustrating Development of Inflammatory and Fibrotic Processes According to Localized Pleurisy Hypothesis (See Text)

Before the localized pleurisy theory can be considered sound, the presence of a shifting fluid level within the annular shadow must be satisfactorily explained. There is reason to believe that this is possible but the condition is a special one, and will be considered after an attempt has been made to explain the mechanism of the formation of pleural annular shadows in general. It is at this point that we must abandon accomplished facts and pass to the realm of hypothesis; but speculation is justifiable so long as it is confined to the zones of reason to which we have already referred. The explanation here proposed is based on a pathological event that is common; otherwise it would not have so much to commend it as plausible.

Referring to diagram 2, it is assumed that the process starts as a simple infection of the pleura at *A*, by lymphatic extension from an underlying pulmonary lesion (*P*), or otherwise. Viewed on the pleural surface, this should be composed of a simple deposit of fibrin, cells and exudate, with or without underlying tubercles (*B*). It is to be remembered that this is not likely to be a pleurisy of the very acute florid type, but rather of the more common subacute or chronic and slowly progressive kind; and any change should, therefore, be gradual, corresponding fairly closely with the degree of activity of the intrapulmonary lesion. Once the pleura is infected, the adjacent normal serosa becomes involved by direct extension from the original focus. It would be expected, therefore, that the deposit (*B*) would slowly enlarge to some arbitrary size which we may represent as *C;* this might require days or weeks for its extension. Returning again to the recognized pathology of tuberculosis, two other principles present themselves for attention. One is that disease of a chronic, slowly progressive type tends to heal as it advances, the common illustration being the lung with fibrosis at an apex and fresh tubercles in a lower lobe. The other is that healing and fibrosis are usually observed first at the site of the older infiltration, the reason that the first cicatrix is usually seen at or near the apex of the lung. Applying these principles to the pleuritic process one should find, in course of time, evidence of healing beginning at the oldest and original focus and, therefore, at or about the centre of the deposit (*C*). The healing would be evidenced by the replacement of fibrin, cells and exudate by fibrous tissue, represented by the cross hatching in *D*. From this point the two processes would progress concomitantly until an arrestment took place. As the periphery of the pleuritic patch extended, involving more and more of the normal serosa, its centre should show progressive absorption of fibrin, cells and exudate and varying degrees of replacement by fibrosis, so that, viewed at any time during its course, the picture would be that of a ring of fresh inflammatory products surrounding a central area of fibrosis (*E*). The latter would in most cases be attached to the contiguous pleural surface (parietal or visceral) by adhesions. Once an arrestment of the process had occurred, the peripheral inflammatory products should be gradually replaced and a general shrinking from contraction of the fibrous tissue would be expected. Finally, the only remnant would be a plaque of thickened pleura, most likely with adhesions; the plaque might be very thin, or heavy and leathery.

Before proceeding further it would be well to hazard an opinion as to the character of the shadow that might be cast in the roentgenogram by this process. The original focal deposit (*A*) would appear not at all, or as a light cottony density hardly distinguishable from intrapulmonary mottling. But, as it extended and its centre became replaced by fibrosis, a corresponding rotengenographic change should occur, as a clearing of the centre of the density, leaving a border of the original light cottony character. Thus, the annular shadow would take form and follow changes corresponding to those described in the actual lesion. It will be recalled that, in the series reported, 78 per cent of the shadows had inner edges better defined than the outer edges and, in the remainder, the definition of the edges was equal, a peculiarity that can be explained on the hypothesis outlined. It is well recognized that, in studying tuberculous deposits in the lungs, poor definition of the roentgenographic image indicates a deposit of comparatively fresh inflammatory products, while clearing of the haziness and sharp definition speak for absorption of these products and the beginning of fibrosis. According to the foregoing theory, therefore, haziness and indefiniteness of the outer border of the annular shadow, presumed to represent recent inflammation, would be expected and at the centre the picture should naturally show some evidence of healing in the form of better definition and more clearly cut edges. The theory would lack in completeness if this relationship did not hold. Since it is assumed that the pleuritic process is subacute or chronic, any mutations in the roentgenographic counterpart should be correspondingly variable and gradual; and finally only the shadow of a thickened pleura should remain: this the investigation has proved to be so. It is also clear that there could be more than one patch of pleurisy and consequently more than one annular shadow in a single case.

If it is to suffice, the localized pleurisy hypothesis must be broadened to explain the shifting fluid level within the annular shadow. Sampson, Heise and Brown hold that this phenomenon connotes the presence of air escaped through a pleural tear. But it has been shown in the preceding paragraph that fluid, contained in a perfect or partial vacuum, will exhibit an upper horizontal level and will quickly shift as the position of the container is changed. This observation demands scrutiny; and so far as this special proposition is concerned, it is our major premise.

If it can be shown that a space, containing a perfect or partial vacuum, can be created between the pleural layers without rupture of the lung, or that such a condition is even probable or possible, then the minor premise is established, and the logical conclusion of the syllogism is that those annular shadows showing shifting fluid levels probably or possibly represent localized separations of the pleural layers, and that in the spaces thus formed small effusions have developed.

The evidence bearing on the minor premise is not abundant, but what there is of it proves the fundamental truth of the proposition. In the stereogram we have seen definite pleural separations and White (17) found from his autopsies at the Phipps Institute that "the two surfaces of the pleura are not (even when the adhesions are numerous) so closely approximated as in a case of obliterated pleura." Evidence that is most convincing and that conforms in detail with the foregoing assumption is found in an article by R. Douglas Powell (19) written fifty-two years ago. The following quotation is from this paper:

> The pulmonary pleura over any portion of lung of impaired expanding power does not accurately follow the parietal pleura; when the ribs are raised and the diaphragm lowered in inspiration a certain gliding or rubbing movement takes place between the two pleural surfaces, and irritation and adhesion result. In cases of disease of the lung leading to toughening and contraction of the organ, there is a tendency to the separation of the two layers of the pleura over the diseased portion and this tendency is increased with each inspiratory effort. The result is a stretching or pulling out of the adhesions which yield gradually and the meshes thus produced are filled up at first by serum mechanically effused, giving rise to the edematous pleura commonly seen in these cases. Secondly, by continued connective tissue growth the whole interpleural space becomes occupied by fibrous tissue, the serum being reabsorbed. Finally, the resistance to expansion triumphs over the inspiratory force, the chest sinks in and the muscles of inspiration atrophy. All these changes, though here mentioned singly, go on together, or at least overlap one another in point of time in an onward series.

This observation of Powell's, based on autopsy findings, is inserted as the logical elaboration of the hypothesis proposed above to explain the formation of annular shadows. He clearly shows how, by contraction of fibrous tissue on or beneath the pleura, the central adhesions in one of these areas of localized pleurisy could be stretched, allowing the formation of an interpleural space with or without fluid. In this vacant or partly filled space there should be a partial vacuum, the degree of which would be a matter of conjecture without manometric readings, but which could not be expected to exceed the normal negative intrapleural pressure; it might be less. The space could not be called a pneumothorax, since this term is understood as applying to the condition artificially induced or resulting from lung rupture but, except for the pleural tear, conditions within the space should be identical with those in a partial pneumothorax or hydropneumothorax under negative pressure. As shown above, any fluid present would behave similarly in either case. Such a phenomenon, then, should present as its roentgenographic counterpart a picture similar in all respects to the annular shadow with a shifting fluid level in its dependent portion. Should the space between become entirely filled with fluid, it would present as a homogeneous cloud with little or no resemblance to the annular shadow. As the fluid, according to Powell's description, is reabsorbed the level would, of course, disappear and this, we know, does happen. Closure of the space would be slow since this is typical of all processes depending on fibrotic replacement and contraction. Once the obliteration of the space had been accomplished

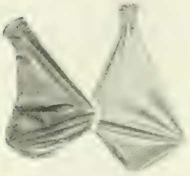

Fig. 5

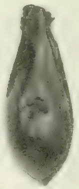

Fig. 6

FIG. 5. SHOWS THE EXPERIMENTAL RECONSTRUCTION OF A LOCALIZED PLEURISY

The attached area of the two balloons represents the central healed and adherent part of the pleuritic patch between the pleural layers, while the strands of horse fibrin placed about this area represent the products of fresh inflammation at the periphery of the patch.

FIG. 6. POSITION IN WHICH ROENTGENOGRAM WAS MADE OF THE RECONSTRUCTED LOCALIZED PLEURISY

The underlying balloon is partly inflated to represent the lung while the overlying uninflated balloon is in close contact to represent the contiguous parietal pleura. The "patch of pleurisy" lies between the two balloons just beneath the pucker shown in the figure. The entire contrivance is bathed in glycerine to give the rubber "serosa" a coating of moisture normally seen *in vivo.*

the only permanent residuum would be, as with the simple annular shadow, a localized area of pleural thickening.

Because of the difficulties in the way of reproducing the conditions of human chronic pulmonary tuberculosis in animals, no attempts have been made experimentally to induce pleural annular shadows *in vivo*; and it remains to be seen whether such an experiment could be successfully consummated. The final conclusion may depend entirely on autopsy reports, but the hindrance here is that, by the time death occurs, the pulmonary involvement is usually so massive as to preclude a roentgenographic study of the more delicate details of annular shadows. It is quite clear also that special pains should be taken to investigate the phenomenon *in situ* before the pleural layers have been forcibly separated.

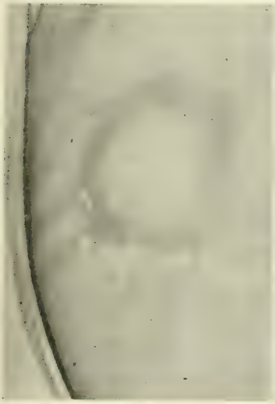

Fig. 7

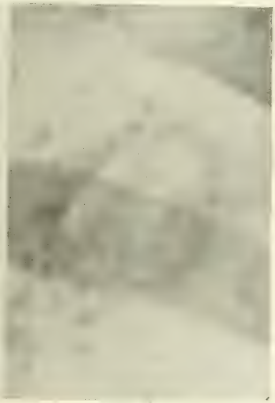

Fig. 8

Fig. 7. Contact Print of Roentgenogram Made of the Artificially Reconstructed Localized Pleurisy Shown in Figures 5 and 6 (Not Retouched)

Note its resemblance to typical pleural annular shadow shown in figure 8. Note the sharp definition of the inner border as compared with the gradual shading off of the outer border. The rarefied areas represent air bubbles purposely included to show the contrast.

Fig. 8. Typical Pleural Annular Shadow Inserted for Comparison with Figure 7

The small heavy densities represent intrapulmonary calcareous deposits.

It is quite simple, however, to reconstruct *in vitro* a localized pleurisy on the hypothesis proposed and this has been done, two small rubber balloons being utilized for the purpose. As shown in figure 5, a circular area on the surface of one balloon was cemented to a similar area on the second. Considering the contiguous surfaces of the balloons as pleural surfaces, the attached or cemented area represents the fibrous and adherent centre of the patch of pleurisy. About the periphery of this area strands of horse fibrin that had been preserved in glycerine were loosely laid, as also shown in the figures, so as entirely to encircle the adhesion and to represent the recent extension of the pleurisy over the serosa and the freshly deposited products of inflammation. The surfaces of the balloons were bathed in glycerine to reproduce the normally moist condition of the pleura. One balloon was then partly inflated and the other uninflated balloon was brought in close contact, so as to enclose entirely the adhesion and the peripheral border of fibrin between the two artificial surfaces or rubber "serosa" as shown in figure 6. The inflated balloon represented the lung and the uninflated one the contiguous parietal pleura, while between the two lay the localized pleurisy, reconstructed in all essential details on the principles of the hypothesis suggested to explain the formation of annular shadows. The balloons were then radiographed while held in the same position as in figure 6, and figure 7 is from a contact print of the negative obtained. Figure 8, a typical annular shadow selected from the series reported above, is inserted for comparison.

Comparing the last two figures, it is seen that they are practically identical in essential details. Both are of a light tenuous character and both have inner borders that are better defined than the outer borders. In figure 7 a few air bubbles have been purposely included, to show the contrast; as compared with other parts of the field, the very small collections of air produce a decidedly rarefied appearance. This experiment does not prove that such a type of localized pleurisy accompanies pulmonary tuberculosis, but it does prove that such a type of pleurisy may cast a typical annular shadow on the X-ray negative and this, of course, is a necessary fragment of evidence.

On the basis of this hypothesis, it can readily be seen why the annular shadow represents a process that, *per se*, does not influence to any serious extent the course of the lung disease. The pulmonary lesion is the primary factor; and its state of activity or retrogression determines the development of the annular shadow as well as the ultimate prognosis of the case. This is theoretically true, and the study indicates that it is practically true.

The merit of probability is claimed for the hypothesis here proposed, to explain the formation of a majority of pleural annular shadows; and at the same time some of the fallacies of the localized pneumothorax theory have been pointed out. This investigation has not attained the final goal, but it has descried an objective that seems to offer some promise. It is believed that the burden of proof is on those who would dispute the hypothesis. A survey of the field of endeavor has been presented, with the hope that others may be spared the efforts of circuitous wanderings and may proceed straightway toward the achievement of the ultimate truth.

CONCLUSIONS

An investigation of roentgenographic pleural annular shadows at the Loomis Sanatorium has shown that these peculiar densities appeared and increased in size as accompaniments of active or progressive pulmonary tuberculosis, and that they decreased in size or disappeared only after the intrapulmonary lesions became quiescent or retrogressive; the converse of these propositions has not been observed. The shadows seem to have no other prognostic significance.

A consideration of clinical, pathological and roentgenographic factors opens to serious doubt the validity of the theory that pleural annular shadows represent localized pneumothoraces secondary to lung rupture.

A hypothesis is proposed to explain a majority of the shadows as the roentgenographic counterparts of simple chronic or subacute localized pleurisies, with or without localized retraction and separation of the pleural layers, and evidence is presented in support of this hypothesis.

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UNDERGRADUATE INSTRUCTION IN TUBERCULOSIS[1]

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In January, 1920, a special department of tuberculosis was created at the University of Virginia in affiliation with a new tuberculosis sanatorium which had been established by the State Board of Health. This sanatorium was located on a site about three miles from the University near Monticello, the former home of Thomas Jefferson. Owing to the fact that the sanatorium was not opened to patients until the spring of that year, practical work was limited to the outpatient department of the University Hospital. During the summer, however, a number of students worked as clinical clerks and assistants at the sanatorium. At the beginning of the last college year the sanatorium had been in operation for six months, was well filled, and the course in tuberculosis instruction was definitely organized, the practical work being transferred to this institution.

It is not necessary to consider here the need for such special instruction in our medical schools or the reason therefor. This has all been discussed repeatedly at former meetings of the National Tuberculosis Association. The work covered by this report is in a way an answer to such appeals. It seemed of interest therefore to give a description of this course of instruction, the methods employed, and the results that had been accomplished.

While some of those who have discussed the question of undergraduate instruction in tuberculosis have held that institutions with ward cases were not necessary, it has been our experience that such material was of the greatest assistance in the systematic presentation of the subject. It was always possible to select at will groups of patients representing certain types of cases, combining in this way demonstration clinics with the more practical, so called Edinburgh method, according to which all cases are worked up by the students themselves, and then presented to the section. Attempts were made, especially at the beginning of each course, to assign similar cases each day, in order to bring out certain features related to tuberculosis, consecutively, and by some method or regular order, instead of taking cases in the order in which they were admitted.

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[1] Read before the Clinical Section at the Seventeenth Annual Meeting of the National Tuberculosis Association, New York City, June 16, 1921.

In arranging the course, most of the work was thrown into the third year. The class was divided into four sections and each covered one-fourth of the college year. Sessions were held three afternoons a week, the session covering from two to two and a half hours. This gave about fifty hours of practical work for each section in addition to the fluoroscopic examinations held once a week at the University Hospital. During the first few sessions of each succeeding section systematic instruction and demonstrations were given in the examination of the chest. The different phases—inspection, palpation, percussion and auscultation, with emphasis on the auscultatory cough—were explained; and the physical phenomena upon which they depend were discussed with the aid of blackboard drawings. Examinations were then made by the students themselves, at first under supervision, in order to correct errors of technique. At each succeeding lesson some new feature was added, in order not to confuse the mind with too many new facts at once.

The principles and methods of history taking were explained, and a schema for the outline of the history given each student for use as a guide. The relation of family history, contact, predisposition. environmental factors, occupations, previous illnesses and former exacerbations, with types of onset was carefully brought out. The correlation of X-ray findings, clinical symptoms and laboratory examinations was then included as part of the examination. The students were expected to be present at the fluoroscopic examinations, in order to hear the description of the shadows as dictated by the radiologist.

Later in the course, as soon as they were perfected in the methods of physical examination, the students were led to compare the recorded findings with the stereoscopic plates and to check these against the official interpretation of the radiologist. In this way the relative significance of the various methods of diagnosis were brought out in a practical way. In order to crystallize the information thus gained, the students made out complete case reports, which were presented to the section in turn, in the presence of the sanatorium staff for further discussion, criticism and comment.

Special topics were selected for discussion, such as the difference between childhood and adult tuberculosis, artificial pneumothorax, various complications like laryngeal and intestinal tuberculosis, the treatment of haemorrhage, the management of cases in different stages of tuberculosis, the classification of cases, the principles of the general hygenic treatment, tuberculin diagnosis and treatment, etc. A number of cases came to autopsy and the anatomical findings were compared with the signs as noted on the charts before death. This enabled the students more readily to interpret physical signs in terms of pathological conditions.

To stimulate study and research, articles from current medical literature were assigned to students for the preparation of abstracts, which were presented to the section for discussion, in which the medical staff of the sanatorium frequently participated.

It was assumed that outside of the above course the third year and fourth year students would from time to time see various forms of tuberculosis in their courses of general medicine and surgery and in the work of the special clinical branches. In order to serve as a general review and to crystallize all this scattered knowledge, a course of six lectures was given at the end of the fourth year, covering the general subject of tuberculosis. Special attention was paid to such topics as the history of tuberculosis during the different periods of medicine, biographical and bibliographical landmarks, its various conceptions, bacteriology and immunology, the tuberculin reaction,the serum reactions, anatomical changes, clinical types, evolution and development of clinical symptoms, with a general consideration of the campaign against tuberculosis, its relation to general and preventive medicine and public health, with a brief summary of the principal statistical facts.

This course of theoretical lectures was then followed by several demonstration clinics, in the course of which it was attempted to show by means of patients in different stages and of different ages the possible history of tuberculous infection in a given hypothetical individual, beginning with a healthy tuberculin negative young child and leading through the stages of the infected but not clinically active process, to the adolescent, young adult, and older adult chronic types.

Shortly after the sanatorium was opened, it was agreed also that the University Hospital would assign one interne from its staff to the sanatorium for three months in rotation. This plan of service worked out admirably. It has been the greatest stimulus to the medical work of the sanatorium to have on its staff a recent graduate, well grounded in the fundamental sciences of medicine, and at the same time in touch with all the recent progress of general medicine and surgery: one who would be awake to note and discover intercurrent conditions and non-pulmonary complications. This interne has acted as the *liaison* officer between the general hospital and the tuberculosis institution. Similar arrangements have been made between the nurses' training school of the University Hospital and that at the sanatorium. The student nurses from the sanatorium have had the advantage of taking the general theoretical courses with those of the University Hospital. Had it not been for the universal shortage of nurses at this period, a rotation service similar to that of the interne would have been arranged, by which the student nurses from the University Hospital would have been assigned to work at the sanatorium. It is to be hoped that this feature will be carried out ultimately.

As far as the work and the interests of the sanatorium are concerned, we are well convinced of the truth contained in one of Osler's essays quoted by Thomas Futcher:

> The work of an institution in which there is no teaching is rarely first class. It is, I think, safe to say that in a hospital with students in the wards, patients are more carefully looked after, their diseases are more carefully studied, and fewer mistakes are made.

It would be premature to judge of the results of our course, but it has been a source of satisfaction to note the interest shown in the work by the students themselves. It was demonstrated in the army during the war that short intensive training courses in tuberculosis were eminently successful, and it would be only reasonable to assume that such knowledge obtained at a time when the mind of the student is most impressionable would stay with him throughout life.

"*The first clinical lessons usually sink the deepest, if imparted methodically, clearly, logically, and with proper explanation of phenomena.*"

SOME PROBLEMS OF MEDICAL EDUCATION IN TUBERCULOSIS[1]

ALLEN K. KRAUSE

From the Kenneth Dows Tuberculosis Research Fund of the Medical Clinic of the Johns Hopkins Hospital and University

An increasingly active interest in tuberculosis has brought about a marked improvement over conditions which existed only a very few years ago. The Trudeau School, the pioneer institution for formal instruction of graduate students, is only five years old. The need and demand for it and its usefulness may be estimated by the fact that applications for enrollment far exceed accommodations, and by the establishment and plans for establishment of similar schools in a number of other localities. The Massachusetts and New York plans of consultation and itinerant clinic services have been notably successful, and enlightening and stimulating to general practitioner and tuberculosis expert alike, and will bear copying and development everywhere. Those in charge of the tuberculosis activities of the Army and United States Public Health Service have been alive to the educational possibilities presented by a wealth of clinical and autopsy material, and have been quick to turn it to effective use. The number of inquiries which one receives from medical schools concerning methods and courses of instruction in tuberculosis is becoming impressive and is, one may hope, highly significant of future development.

Many indications, therefore, point out that we are already well along, —further along, perhaps, than we think. It is, at the same time, only too apparent that many changes, something of the nature of a reconstruction —of methods, of standards, of values—must be brought about before we may admit that we are making the most of our opportunities or that we are teaching tuberculosis with anything approaching complete effectiveness, yet there should be little doubt that a standard of perfection should always be our model; nor, for this reason, should I be inclined to defend any ideas which I may present against the criticism that they comprehend a standard of perfection. Appreciative of all that has been done in the way of education in tuberculosis, I am vastly more interested in whatever will make tuberculosis an object of productive study and teaching wherever the physician comes in contact with it.

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[1] Read *in absentia* before the Clinical Section at the Seventeenth Annual Meeting of the National Tuberculosis Association, New York City, June 16, 1921.

Individual ideas of what constitute problems of education in tuberculosis are likely to be colored by two prejudices. These arise from the personal attitude which everyone of us has formed toward the age-long controversy over the purpose and direction of education in general, and from those particular interests in tuberculosis which your or my study and practice of it have brought out and developed.

Any one of you may intuitively disagree with whatever position I may take on whether the general purpose of education should be to fashion personality or to perfect machinery—to spread before the plastic intelligence the accumulated stores of all sowers and reapers of the past, or to take the twig at its first budding and incline it in a definite and special direction. The question will never be settled; and, after all, why need it be? — for the pathfinders, the seers, the geniuses, the "self-educators," resisting all discipline, conforming to no rules or systems, whipped on by irresistible impulse and spurred to colossal industry, will lay at our feet what our planned endeavors with thousands have failed to produce.

For the moment I forget who it was—perhaps it was Kant—who said that in teaching he was concerned only with average men, inasmuch as there was no hope for fools, and geniuses would take care of themselves. We may or may not subscribe to this view. Yet it is quite likely true—or at any rate practical—that, when considering the persons to be taught, we should keep our eyes fixed on the needs of the average man. As a routine procedure, it would be as foolish and mistaken to prepare banquets for Louis Pasteurs as alphabet noodles for our Sabbath entertainer, Mr. McNutt.

Any educational plan requires that we give earnest attention to something more than the needs of the student. This something is comprised in the best interests of the subject to be taught. And, although the needs of the student and the best interests of the subject may not be capable of dissociation, it is my diffident opinion that, in approaching the matter of education in tuberculosis, we are under far greater obligations to think and act from the point of view of what may be best for tuberculosis—what will ultimately advance the knowledge and science of tuberculosis—than to any course which may promise to be immediately practical, enlightening and advantageous for the student. I have no doubt that, in our life-time at least, students will come and go while tuberculosis will maintain its rôle of the poor in our midst. I have just as little doubt that the more quickly and more securely tuberculosis takes a higher rank among the scientifically-pursued branches of medicine, the more it will attract a larger body of able students and investigators. As I see it, the best interests of all concerned—patient, student and practitioner—demand that the lines of tuberculosis study and practice be tightened all around, that requirements for both the latter be raised and made more difficult, not simpler.

I am constrained to state this for two reasons. The first is that I am continually being reminded that the average internist does not entertain a particularly high opinion of the medical knowledge and ability of the professed practitioner and student of tuberculosis: and, while you may say that we reciprocate the feeling, this retort does not alter or amend the situation. Besides, it is our own knitting that we are primarily concerned with.

The second reason is the free and easy—I almost said, irresponsible—conception of tuberculosis teaching which many seem to hold. If I have understood them correctly, I have gathered from not a few contributions on the subject that, by playing the stethoscope over certain infallible areas of the chest for an hour or two a day throughout a week or two, yokels are converted into diagnosticians of tuberculosis; or that a few easy tricks with the fluoroscope and the acquirement of a catchword or two will open up the realms of pathology, etiology, diagnosis and prognosis; or that fifteen minutes with motion pictures will accomplish what formerly "took twenty-four lectures of one hour each;" or that a demonstration of how to stain the tubercle bacillus and how to inoculate it into a guinea pig makes an investigator out of a novice. Now, all this may be true; yet I can't believe it. Perhaps the fault lies with me, as I am led to survey my own deficiencies and inefficiencies as a drill master. Yet I am encouraged to take heart as I reflect on the possibilities that might arise out of a case, up for opinion, before Webb and Minor and Brown and Hamman and Baldwin and Miller:—when I consider the six different histories, the six different exercises with the stethoscope, the six different X-ray plates,—and then the weighing of all the evidence in the balance of six individual experiences,—and finally the opinions as to diagnosis, and after diagnosis as to what is to be done with the case, and then—all important perhaps, for the patient and his family—the prognosis. I verily believe that, if what many have told us about the shortcuts to a knowledge and practice of tuberculosis is true, the event would show that these six eminent practitioners had flagrantly abused their opportunities to learn or had been singularly refractory to newer, sureshot methods.

Now, tuberculosis should and must be taught to medical students, to medical practitioners, and, perhaps, even to patients; and it is our job to devise ways and means to teach all three, practically and effectively, while we at the same time send tuberculosis along as a developing and attractive subject. It takes comparatively little wit—or conscience—to set down on paper comprehensive and ideal courses. I have already done this several times and expect again to commit the same misdemeanor before tuberculosis and I finish it with each other. It is easy to pass resolutions, even with one's self; but discouragingly hard to make them work, no matter how embellished they may be. At the present time I shall put aside the temptation to reissue a programme of instruction. I had rather point out problems which may confront the practical working out of programmes.

Let us consider, first, the case of the undergraduate student. What would you have him do?

Throughout the literature there is distributed an enormous amount of gloom over the new graduate's inability to make a diagnosis of pulmonary tuberculosis. But is it justified? I'll grant that a fourth year student who fails to detect the disease because he does not know how to find bacilli in a positive sputum, or who "misses" the cadaverous consumptive who is so plain that his lay home associates have no doubt that he "has the bugs," has been inefficiently instructed or is a numskull. But to expect him to proceed in a business-like way to make a diagnosis of a difficult or questionable case of lung tuberculosis is as irrational as to trust yourself to him for the removal of your appendix or your brain tumor. Beyond their veriest rudiments the technique and judgment of tuberculosis diagnosis can no more be acquired by the average undergraduate student than can surgical technique and judgment. If tuberculosis—in any of its phases—were so easy as some would have us believe, it would not have long ago become a special branch of internal medicine. Everyone of us here has sweated—and is still sweating—to gain what little he knows about tuberculosis—throughout the long years devoted exclusively to tuberculosis. Then why be so hard on the undergraduate or so contemptuous of his training? The quicker we appreciate that physical diagnosis cannot be learned from didactic lectures, or parallel columns of signs, but that competency in it can be attained in only the same way as a proficiency in operative surgery, that is, by assiduous observation at the autopsy table and practice on the living patient—just as Laennec erected its foundation—the sooner we'll be in line to formulate plans for the most effective instruction in pulmonary tuberculosis, especially for undergraduates.

It has no doubt happened, not infrequently, that Professor X., new head of the tuberculosis department, animated with all the enthusiasm that whole-hearted devotion to his subject can give him, has entered the faculty meeting which is to plan the curriculum for the coming year. Passionately determined to see it through, he sits down with a course of instruction in tuberculosis which he is convinced represents the minimum that a medical student may be given before he may be turned loose upon the public. Around the same table are a dozen or score of other heads of departments. Professor A., of genitourinary diseases, hasn't the least doubt that a medical student who cannot cystoscope a man with comfort and profit to the patient is unfit for graduation. Professor B., of pediatrics, considers that graduate a menace to society, who, when first called in, might confuse chickenpox and smallpox. Professor C., of laryngology, insists that, since adenoids, enlarged tonsils and other nasopharyngeal affections are the most common disabilities of human beings, he must have a full third of the student's time to impress the latter with his responsibilities. Professor D., of ophthalmology, makes out a strong case when he points out that the normal human eye exists only in the textbooks and that the least he can expect of the student is his taking a full course in refraction: he may waive instruction in minor complaints like pink eye and leave this to the pediatrician. And so it goes—from anatomy to X-rays—with the professors of the two major subjects of medicine and surgery silent and wondering how they are to squeeze in an occasional hour to tell the student how to treat a headache or a boil on the neck.

The result is a compromise; or once in a while, if you will allow vulgar but expressive terminology, a "freeze out." Professor X., if he has his wits about him, is brought to see that medical education to-day is concerned with a great deal besides tuberculosis, and that, in a school of medicine, there are even some reasons for looking upon a tuberculosis department as exotic and a luxury. I bring up this particular situation as a problem because it is a most real and practical one, yet one which most homilies on what should be taught undergraduate students in tuberculosis have overlooked.

Problems of another nature arise when we attempt the tuberculosis education of graduates, who are usually general practitioners. We have long been aware that many of these men were clamoring for a better appreciation of our most common affliction: and in response to an insistent demand it has become fashionable to organize schools for "intensive" instruction of tuberculosis. These schools pretend or essay to range the field at large, and in six weeks at the longest place before the student the totality of our knowledge of tuberculosis. Tuberculosis in children is covered in an hour or two, while the larynx, the bones and joints, the genitourinary system, the meninges, the peritoneum and intestines, receive as much or less attention. One morning will generally "clean up" the bacteriology of the bacillus, and another morning the pathological reactions to the bacillus. There are demonstrations and drills on signs and symptoms, with fleeting interludes of institutional management and the social phases of tuberculosis. The paper plan of some of these courses is almost a transcription of the table of contents of Cornet's book, and if anything is missed I have failed to detect its absence. All this in six short weeks and less!

I would be the last to dispute that in experience and judgment the man who has practised medicine has a very definite advantage in assimilating knowledge over the immature undergraduate. Yet I consider it arguable whether this advantage may not be offset by the enthusiasm, the plasticity and the quickness of perception which are more common to younger minds. And I seriously question whether this cramming process of "intensive" instruction of graduate schools is serving the best interests of either student or education in tuberculosis. A student with a fair knowledge of tuberculosis can no doubt profit much by the course and have his ideas orientated and crystallized. But the student without such preliminary knowledge—and he is one of the majority who take these courses—must run the danger of stepping from the crystalline atmosphere of ignorance to a murky one of intellectual fog. I had rather see the average graduate student put on one case and on one sputum and one cadaver or pathological specimen and one infected guinea pig and one culture until, with his instructor, he had exhausted the possibilities of each, than continually transferred from one sketchily presented subject to another. I believe that this method would turn out wiser and more effective men. It might look less showy in the prospectus and appear less popular to those unfit and unprepared practitioners who were accustomed to *gaze upon* the wealth of Vienna clinics: but effectiveness in education must be estimated, not by the mass that is presented to the intelligence, but by the growth which the intelligence has assumed.

Four years ago I spoke at an annual meeting of this Association on Undergraduate Instruction in Tuberculosis. Before leaving for Cincinnati I read my address to Doctor Theodore Janeway, a man of broad experience and vision. I was in the midst of reciting apparently essential details for the proper training of medical students, and among other necessities came upon the phrase "an able and enthusiastic teaching force;" when Janeway interrupted with, "Ah, that is the heart of the whole problem. Where and how are we going to get the able and enthusiastic teachers?"

Since then my time has been continually and exclusively occupied with tuberculosis work, much of which has had to do with the education of students, both undergraduate and graduate, and of the public. Perhaps no part of it has been so beset with what seem to me unsolved difficulties and problems as this one of education. And in reflecting upon them I usually find myself coming back to Janeway's query, "How and where are we going to get able and enthusiastic teachers?" To me "able and enthusiastic teachers" mean men who before they essay to teach are thoroughly grounded in tuberculosis; men, also, who are making of it their life study; men capable of conducting investigations, and with the time at their command to do so.

Our potential sources of tuberculosis teachers would seem to be the medical schools, the sanatoria and the small body of practising and consulting physicians who are making of tuberculosis—usually pulmonary tuberculosis—a specialty. To the uninitiated it might seem a simple matter to call upon men from all three sources and put them to work at teaching tuberculosis. But a very incomplete survey of conditions as they exist at present will at once bring to light many handicaps which would hobble any efforts to build up a strong body of men who are to devote their lives to the teaching and scientific pursuit of tuberculosis, both of which occupations are in my mind, inseparable requisites for real effectiveness.

So far as medical students are concerned, you will no doubt grant that their instruction must proceed in the medical school or under its auspices. Our newer and more solid ideas of infection, immunity, symptomatology, diagnosis, latency and activity, therapy, etc., point out with increasing emphasis that tuberculosis is a subject which comprises vastly more than the diagnosis of its pulmonary phases and the treatment of special classes of these. Only in medical schools connected with large general hospitals can we expect to come in touch, even approximately, with tuberculosis as a whole. The function and the opportunities for observation in almost all sanatoria are, after all, very limited and very special. Almost all their inmates are referred patients, with diagnosis already made, and represent usually a few selected more chronic types of disease. A man may spend a lifetime at a sanatorium, be looked upon as an expert in tuberculosis, and yet never called upon to make what is now and again the most difficult of diagnoses, namely, that of acute tuberculous pneumonia or miliary tuberculosis in a previously healthy adult. Yet this is the common contact of the general hospital ward with pulmonary tuberculosis, and brings into play diagnostic qualifications which the *average* sanatorium resident has not had the opportunity to acquire.

The X-ray department of a large general hospital will make observations on as many as twenty thousand plates a year, depicting every variety of pathological abnormality occurring at every age. It is to be expected that the same man will gain a much broader and a more exact idea of the roentgenology of tuberculosis in a general hospital than in a sanatorium; and the fact that in the former his impressions will quite often be tested by an autopsy will contribute to his poise and carefulness of interpretation.

The question of tuberculosis as against other affections comes up daily in the children's clinic, and now and then you will be fortunate enough to observe the clinical disease develop under your eye in children whom you had previously had under observation for measles, pneumonia, etc. The masked phases of tuberculosis, as they present themselves to the dermatologist and ophthalmologist, call for thorough investigation from the point of view of foci elsewhere in the body. More marked manifestations, which come to the attention of the orthopedist, the urologist and the general surgeon, present the same opportunity. The tuberculosis dispensary has its own unique problems of diagnosis and treatment; while the hospital pathologist will show you tuberculosis where it was never suspected during life and no tuberculosis where you had positively proclaimed its presence.

Now, with all these opportunities to study and teach tuberculosis as a whole—and this is the only truly effective way to handle the subject

—there is not a single medical school or university in this country which has shown itself fully alive to the possibilities of developing the scientific side of tuberculosis. There is not even a single adequate, *permanent* foundation in tuberculosis. The result is that there is no inducement for the better class of men to go in for a career in tuberculosis, with the further result that we can develop few able teachers in the subject.

What attracts eager, young minds with a passion for study and investigation to enter upon a scientific medical career? It is, besides the facilities and opportunity for work, the possibility of ultimately attaining a position of dignity and influence in their chosen work. This is, and always will be, the incentive: the opportunity to make money, to "cash in," will always be subsidiary and when it comes and is grasped, it usually plays havoc with a man's usefulness as an investigator. Without the incentive I have mentioned we can look forward to but little advance in real tuberculosis education; for we will not be in the position to train teachers of the same grade, say, as those who now occupy our chairs of medicine, surgery, pediatrics, etc.

Let me put the case a little more pointedly. I direct a department in tuberculosis. Its primary object is research. In it is also a dispensary, and it teaches students by clinics, lectures and first hand demonstrations of patients. It has, moreover, desk facilities for the laboratory training of a few students.

Now, suppose a man comes to me, fired with the idea of devoting his life to the study of tuberculosis. He wishes to train under me. What, in all honesty, am I to tell him? Why, I must talk to him something as follows: "You are welcome to every facility that is here and I shall give you every aid. But I really don't know what to do with you if you make good, if you gain a mastery of your subject and show talent for furthering it. On the other hand, I don't want you if you are going to fail: and if I knew or thought that you will fail, I should not take you. Yet, if you do make good, where is there a position for you? If you should go into medicine or surgery or gynecology or pathology or any one of a dozen other branches, there are a full score of decent professorships in each, any one of which may in time come to you, provided you play the game and make the most of your abilities and opportunities. Now, I have watched you and have thought that you may have a special talent for tuberculosis work; yet at present I really can't see what's ahead for you except my own job and it is not on any too secure a basis."

I have made this kind of a speech, not once, but several times within the last few years: and I have made it with a gripping at the heart. I have turned men away, have seen them lost to tuberculosis, simply because I could not see ahead of them an adequate career in tuberculosis. Almost any other branch of medicine was open to a display of their talent, —but not tuberculosis. And remember, please, that I am in a peculiarly favored position.

This situation would change over-night if we had foundations—departments of tuberculosis—in our medical schools: it will not change until we do have them. I should say that in medical schools like Columbia, Harvard, Pennsylvania, Chicago, Johns Hopkins, etc., an adequate foundation would require resources netting $50,000 a year.

This is, indeed, the very heart of the problem of tuberculosis education. With permanent tuberculosis foundations, investigators and teachers would soon spring up. Many would come over from pathology, bacteriology and clinical medicine. Many scattered phases of tuberculosis in general hospitals would be coördinated and harmonized. Above all, students would be taught tuberculosis as a whole. It surely should not be necessary for me to detail what all this would mean to tuberculosis. Suffice it, that tuberculosis would take its place as a branch of medicine, acknowledgedly on a scientific basis.

If we go to the sanatoria for our teaching and inspiration, what do we find? In trying to answer the question I wish to be particularly honest and fair, and trust that I may not be too lavish in either praise or censure.

As I see it, there are invested tens of millions, supporting hundreds of institutions, taking care of thousands of patients who offer a most fruitful field for the study of tuberculosis which is hardly cultivated. The apparent apathy and lack of interest manifested by the medical staffs of sanatoria in the study and investigation of tuberculosis must be the despair of the well-wisher for tuberculosis. Here are hundreds of men, surrounded by a wealth of clinical material, yet real study of it is so uncommon that a sanatorium resident who publishes a paper now and then, at once and because of the fact, is regarded as an unusual man.

I have asked many why this lack of initiative and investigative morale exists in the sanatoria; and have received various answers. Some men tell me that the present organization of the average sanatorium and the duties of its medical staff leave little time for study and thought. If this is true, then the quicker we bring it about that the resident physicians are relieved of the responsibilities of business managers and stewards the better it will be for institutions, for patients and for tuberculosis.

Others tell me that the very location of many sanatoria and the usual method of recruiting their medical staffs work against the development of lively and active interests in study and discovery. For very good and sufficient reasons, sanatoria are frequently placed in isolated places. Their medical staffs are thus cut off from that close association with their confrères which is so stimulating and so necessary, if intellectual stagnation is to be avoided.

Again,—so they say,—many, many sanatorium men are physically weak and medically weak. To be physically weak, within certain limits, does not necessarily mean that a man cannot do good work; it does not mean so, if within him there burns the passion to develop those talents of mind and soul which physical weakness quite often gives unusual chances for exercise. Somewhere in one of George Gissing's essays, there is a phrase that runs something like this: *that the man of thought is almost of necessity a man of impaired health.* And our own Trudeau, or Kant, or Florence Nightingale, or Charles Darwin, or a host of thousands of others of the world's great in all ages, bear witness to the eternal truth of Gissing's statement.

I am not so sure that a general indictment of "medical weakness" against our sanatorium staffs could be sustained. Nevertheless, it is noticeable that many of our residents, before taking sanatorium positions, have had no more training in general medicine than that afforded by an undergraduate course, and that frequently this has been interrupted because of illness. Personally, I think that, if too many men of so little preliminary training hold posts of responsibility in sanatoria, it cannot be otherwise than bad for tuberculosis. There are, of course, exceptional men who will come through despite every handicap and deficiency of background; but, as a general thing, I am inclined to question seriously the voice of authority in tuberculosis which has assumed eloquence because of a superstructure of sanatorium experience on a cornerstone of an ordinary or crippled medical course. Too exclusive an attention to pulmonary tuberculosis with little or no acquaintance with general medicine is bound to give us a false tuberculosis; which might be worse than the ignorance of tuberculosis that would mark the general practitioner who shuts his eyes to tuberculosis as a phenomenon to be reckoned with.

Wherever the trouble may lie, the fact remains that too little study is going on in our sanatoria and too little solid work is coming from them.

And if anyone were to ask me how the situation might be bettered, my instinctive reply—and I hope Lawrason Brown will pardon me and allow me to make it—would be, "Go see Lawrason Brown." For I consider that in ten years of residence at the Adirondack Cottage Sanitarium, under conditions which I know were not always rosy or ideal, Brown demonstrated what can be done with sanatoria as centres of investigation and development of tuberculosis. Further, I cannot see why Brown's example in this respect cannot be followed in scores of institutions throughout the country, yet the list of sanatorium men who have attempted to use their institutions as places for *sustained* and productive study is lamentably small.

A man who is not interested in study is not a fit teacher; or, if this statement is too extreme for you, then a born teacher, who develops tastes for study and investigation, becomes an infinitely better teacher. Teaching consists in something vastly more than unbosoming your knowledge to the student. It demands that you have within you that interest and passion in your subject which will inspire your student and goad him on to self-development: and this interest and passion can be kept alive only by study and investigation.

Such then, sketchily and imperfectly presented, is the situation as I see it. I have tried to go to the root of things and discuss what appear to me as fundamentals. This has no doubt made me censorius, and indulge a spirit which is furthest from my intention. Let me remind you, though, that my own life's work is wrapped up in this matter of tuberculosis instruction, that I have tasted of its possibilities, that I too am beset with difficulties which are far from solution, and that I am trying to find a way out.

The sum and substance of my own view of present problems of tuberculosis education are that (1) we should not expect too much from instructing undergraduates, because of the great diversity of topics which now occupy their time, nor should we lay too much stress on physical diagnosis in particular, since an expertness in this cannot be acquired from facilities now open to students; (2) short courses for the common run of graduate students require great simplification, elementary thoroughness and concentration on several—perhaps a very few—particular objects; (3) the heart of the problem is the building up of a body of able teachers; and (4) it is doubtful whether, with relatively few exceptions, able teachers in tuberculosis can be recruited from either medical schools or sanatoria under existing conditions.

If you ask me for solutions, then I would reply that I have none ready. Yet I believe that with definite objectives before us of what we wish to correct and achieve, with no illusions as to the time or trouble that it is going to take us to achieve our purposes, and, ever hopeful and thick-skinned against discouragement, with a long and strong pull working all together, we can work out satisfactory arrangements and send tuberculosis far.

We should at once begin to take measures to plan departments of tuberculosis in medical schools and to raise requirements for medical internship in sanatoria and standardize sanatorium management, the last object of which means that a medical director should be engaged with medical matters and with nothing else.

We should decidedly get more general medicine into sanatoria and more tuberculosis into general medical schools. I can see nothing to prevent working arrangements for fortunately situated institutions, whereby sanatorium residents may spend part of their time in general hospitals, while hospital residents and medical students similarly put in a month or several months a year at sanatoria, and whereby the several institutions may exchange teachers and laboratory workers.

I have rather grandiose visions of the possibilities of sanatoria in education, just as soon as the morale of their staffs is uplifted and tightened all around and their functions are broadened as I have attempted to point out. I hope to see them centres of investigation and of solid instruction in tuberculosis to physicians roundabout. The time is almost ripe for sympathetic bodies like the American Sanatorium Association and the National Tuberculosis Association to undertake an exhaustive and constructive inquiry into how the scope of tuberculosis sanatoria may be broadened and improved, especially from the point of view of education and scientific activity; for, with the millions invested by the people in sanatoria and in the face of a growing murmur that sanatorial functions are very limited and that the institutions are not giving results proportionate to value receive, it is inevitable that if we do not make the survey, if we do not take hold of the reconstruction, less charitable interests will demand the right to do so.

And, as a parting observation, I would point out that tuberculosis, as an attractive and interesting field for study and training, will appeal to physicians and students alike, in a measure that is directly proportional to the devotion to study and productiveness in investigation which those at any time identified with tuberculosis exhibit. The animal man, the general public, is just so "cussedly" constituted that the business of resting on one's oars will not excite him: he delights in and is enthused and motivated by action. The moment a reputation becomes static, that moment it enters upon its descent to obscurity: growth comes only through feeding and strength through exercise.

THE TUBERCULOSIS PROBLEM

SOME THOUGHTS ON ITS SOLUTION[1]

ALLEN K. KRAUSE

From the Kenneth Dows Tuberculosis Research Fund, of the Medical Clinic of the Johns Hopkins Hospital and University

Everyone of you knows the score of tuberculosis: an intolerable evil, because of its millions of preventable deaths; an enormous waster, through its withdrawal of millions more of people from productive life, its economic wrecking of innumerable homes, and its tax on us for the relief of the disabled and impoverished; and an ever-menacing peril, obscure and furtive in attack and development, and deceptive and treacherous in its course.

As long as the weight of opinion documented tuberculosis as an affliction which was inescapable for its victims and transmitted from parent to child through a constitutional vice, society could afford to be indifferent to every one of the countless tragedies and disasters with which tuberculosis splotched its multicolored fabric Indeed, society had no other way than to survey with folded hands the ravages of the disease, as the members of society were wont to examine nervously their family trees and take comfort or alarm therefrom.

The moment that the scientific world accepted Villemin's demonstration of the infectiousness of phthisis, the identity of scrofula with tuberculosis, and the relationship of the pearl disease of cattle with human tuberculosis, the attitude of society began to lose something of its passivity. It awakened to the fact that it could resist. And when, a few years later, Koch placed before men's eyes the actual cause of the disease, society turned to fashion the weapons of resistance.

Not even the wisest seer can ever comprehend the full importance or ultimate effect of the most insignificant discovery. Truth discloses itself grudgingly and never, at any time, more than partially. Little by little it comes to our senses and, variously interpreted, takes its place in consciousness; and, if the past teaches anything, this is that every new secret wrung from Nature makes necessary a revision of our conception of its last revelation. At the same time, we are prone to use the truth according to our prejudices and habits of ratiocination;—habits laid down through all our ages of ignorance. To us, tuberculosis would seem a perfectly hopeless and insoluble human burden, if we believed it wholly, or for the most part, to be on an inherited basis. Yet, to at least one of Villemin's opponents, the idea of contagion made the situation one of utmost despair. Pidoux, of the French Academy, was no doubt wholly sincere when he attacked Villemin's experimental proof with the following sentimental broadside:

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[1] An address delivered under the title, "Solving Tuberculosis, a Many-Sided Problem," at the open meeting of the ninth session of the Mississippi Valley Conference on Tuberculosis, Columbus, Ohio, September 12, 1921.

> What a misfortune if things should turn out in this way! Social economy, private and public hygiene, prophylaxis, medicine—all condemned beforehand in their aspirations and their efforts! The poor consumptives sequestered like lepers! Family affection at war with fear and selfishness, against a disease whose protracted course and homicidal atmosphere bid fair to wear out devotion! If phthisis is contagious, we dare not say it aloud.

From that day to this we have said it aloud; in tones which would seem vociferous to Pidoux; in terms, however, which have shifted with increment of knowledge and have been revised and readjusted to fit in with each new bit of information. Meanwhile, families have held together; and medicine, prophylaxis, and private and public hygiene have flourished with renewed vigor.

All of you are again familiar with how hard the road has proved to be since Villemin's and Koch's time. I imagine that to the enthusiasts of thirty and forty years ago it suddenly broke into view straight and direct, an open path across the maze of existence. There was a disease, consumption. Many adults, but few children, had it. It was contagious,—in somewhat the same sort of way as diphtheria was contagious. People came in contact with other consumptives, at home or abroad, inhaled the germs and, not long afterward, fell ill with cough, fatigue and fever. Their physicians now had an easy method of discovering tuberculosis in them: a sputum examination would tell the tale. Brehmer, Dettweiler and Trudeau had shown how remarkably consumptives responded to measures of treatment.

The tuberculosis problem was made up of a few simple elements, all easy of attack. Detect consumptives by examining their sputum.

Treat them in sanatoria and cure them. Their constantly diminishing number will in time remove the sources of infection. Only consumptives have tubercle. Therefore, clean up every consumptive's surroundings and cook animal food, for these are the only sources. And, while Bayle in 1810 had called attention to quiescent tubercle in those in whom it was never suspected during life, and Laennec had warned of the dangers of false convalescences, or relapses, most men had forgotten this.

To drag into the light the truth about tuberculosis, to make still more simple the problem, to find the cure and the preventive, and to cut off infection, workers swarmed to its study. Events crowded thick and fast. And, while the specific and the preventive and the cessation of infection yet remain to the achievements of the future, few diseases have been so fruitfully and profitably studied. In a short time we have gathered a body of knowledge concerning tuberculosis that, despite unanticipated difficulties in its pursuit, is singularly authentic, and exceeds perhaps that of any other major disease. It has taught us more about the etiology of tuberculosis than we may affirm about our common, transitory, self-limited infections, which should apparently be much easier of solution. It has refined diagnosis of a disease of protean pathological manifestations to a point which is unique in infections: nor would we here, without argument, except the case of syphilis. It has made possible the detection of infection at a time that is long antecedent to its manifestations. It has given us peculiarly exact standards for the accumulation of epidemiological data. It has provoked the contrivance of prophylactic measures which public hygiene in general is using with telling effect.

The trouble is not, as some would have it, that we do not know enough about tuberculosis. We cannot know too much about any menacing condition that confronts society: and we surely do not know everything about tuberculosis. So much is certain. But to me it seems rather that our present predicament, if (as some assert) there exists one, proceeds from a jumble of uncrystallized, unassimilated and imperfectly applied knowledge. We suffer from an excess of wealth which calls for better bookkeepers than our feverish quest of the lodestone has given us time to train. Bent on stumbling upon the nugget, we have been blind, only too often, to the meaning of the finer grains that have come to hand. Yearning for formulas, for concretes, for catchwords even, we have not got down to nor encouraged the sifting of basic principles from masses of conflicting data which have grown to discouragingly enormous proportions.

For, in no single phase, does tuberculosis present as simple an aspect as imagined by the pioneers. As concerns its social relations, its place in nature, it is time to stop looking for simples in tuberculosis. Every new fact during the last forty years has all the more loudly called out the warning for us to beware of the man who can perceive only one method of infection, one cause of onset, one diagnostic sign, one infallible test of prognosis, one method of prevention, one factor of resistance, one means of cure of tuberculosis. The bases of tuberculosis are almost as broad and large as its effects; its own *mise en scène* as variegated as that of the world in which it plays its part and which it reflects. Its effects reproduce its causes; and give birth, as well, to many nonspecific and apparently unrelated conditions which in turn propagate more tuberculosis.

Gradually we pushed back the onset of clinical tuberculosis from the observation of germs in the sputum to the detection of certain signs in the chest. We made the ferreting out of the early cases of tuberculosis the centre of our combat against it. As a first step, the physician had to be taught a new mechanism of diagnosis and its meaning. In time, however, we learned that many undeniably healthy people presented these infallibly diagnostic signs, and not long afterward became aware of the widespread incidence of infection in those who were not in the least danger of falling ill with tuberculosis. Diagnosis and etiology began to take on new values. When is a man ill with tuberculosis? Is it his signs, his symptoms or his history that should send him to the sanatorium? Physicians will still disagree on these two questions, but the old dictum of the earlier the diagnosis the better the chances of lasting cure remains unimpaired.

Appreciation of the universality of infection made inevitable a more critical examination of our views of infection and etiology. It was hardly credible that everyone had been in direct and intimate contact with a consumptive—the idea of infection twenty years ago—or had ingested infected cow's milk. Only a more catholic view of the possible methods of infection could fit the facts.

For most of us, ordinary single and isolated incidents of infection are likely of slight moment. The etiology of manifest tuberculosis disease is more and more regarded as bound up in two factors, namely, unusual opportunities for repeated infection and unfavorable environment. What constitutes an unfavorable environment is, in general, understood accurately and in detail: and, just as it may swing the balance in the arrested case toward relapse, so it determines disease in the harborers of infection who, in better surroundings, would keep their infection quiescent. What proportion fall ill because of repeated infections and what proportion because of debilitating environment cannot be estimated; but all signs point to the latter as the more active influence.

Thus the facets of our tuberculosis problem have continued to expand and to multiply: we could go on, and cite instance after instance of the light of new discoveries throwing its rays upon new and unexpected contingencies. We now reëmphasize what has become an old story. Infection, of itself, is relatively unimportant—broadly speaking. The problem of preventing the outbreak of frank disease in the legions of the infected is the crux of the programme of prevention; and, in the whole scheme of tuberculosis, yields first place to only the pressing duty and necessity of providing means to restore to health those already ill.

It is when we come to follow this phase of tuberculosis that we gain some realization of the true place of tuberculosis in our daily affairs and the delicate interrelationships between it and society. More or less poverty in a community will mean more or less tuberculosis: so will more or less crowding and improper housing, more or less hygienic occupations and industry, more or less occurrence of other diseases, particularly respiratory infections, etc. Under the circumstances our duty, our programme, is plain and permits of no equivocation. It is to contribute to the attainment of civic decency and cleanliness; of light, space and food enough for all; of a rational proportion of working and leisure hours for those who cannot dispose of their own time; and of the reduction of preventable infections to a minimum.

The solution of the tuberculosis problem is, therefore, partly dependent on the removal of other evils and inequalities which constitute, no doubt, a more fundamental social problem than does tuberculosis itself. We may not at all times be able to fall in with the propaganda that aims to arouse man to the accomplishment of apparently remote objects which would undoubtedly have a direct, though unintended, effect on tuberculosis. Time and again, in the welter and narrow provincialism and chauvinism of issues, I certainly cannot. Yet there can be no question as to what direction our sympathies and activities as tuberculosis workers should take. They must ever be enlisted in whatever makes for equality of opportunity, intellectual and material: they must strike at civic neglect and pillage: they must bring home to the people how inevitably is tuberculosis the child of their dirt and darkness and deprivation of the comforts of life: all this after individual responsibility is given its place; and all this, too, with the strict proviso that as a health organization we dare never become involved in politics or in class conflict. It is for us to point out the way as concerns tuberculosis: it is suicidal to our cause to allow our devotion and enthusiasm to outrun our whole responsibility to mankind. I may, for instance, look upon tuberculosis as a terrible evil, yet I should regard the abrogation of certain fundamental Anglo-Saxon rights or the disruption of some features of our social and economic structures as far greater catastrophes, even though it could be shown me that the latter would surely bring about the abolition of tuberculosis.

We have been going ahead. With never a thought about tuberculosis, society has contributed to its decline. If you doubt its decline, read the mortality returns for the last few years. Bunyan's designation of consumption as "the captain of the men of death" no longer holds—in this country at least—and we speakers on the subject have thus been deprived of our thriller of an opening phrase.

Without reckoning on tuberculosis, society has slowed its sweep in many ways. The demand of city dwellers for better and cleaner streets, for parks, for public utilities within the reach of the poorest, for public schools which make your and my old ones seem like pesthouses, for medical inspection of schools—in short, for something in return for their taxes; the revolution—for it cannot be called less—in factory and office architecture and in plumbing for every purpose; the remarkable suburban development of our cities; the new principle and policy of vacation periods for wage earners; the unparalleled vulgarization of good dressing and many changes of clothing, with its attendant cleanliness and psychic uplift; the astonishing increase in popular amusements, with a coincident diminution in household "chores" and labor; the extraordinary expansion of private and industrial insurance, which has mitigated economic shock for millions of dependents: all this, and much more besides, can have had no other effect than to aid in fending off tuberculosis. It has more than balanced provocative factors, such as the ever growing trend of the population from country to city, the immeasurably better facilities and the cheapening of the means of communication, and the far greater speeding up and strain of modern industry.

It is plain where our duty and our work as tuberculosis campaigners lie. It must be evident to all of you that increase of comforts, of leisure, of food, of space, of the individual means to obtain these, can come only from increased wealth which, whether we approve or not, results only from increased productiveness, And, while attempts to push production may, *per se*, involve the very strains and hazards that bring on tuberculosis, it is for us to get behind and encourage every ameliorating factor at the same time that we are trying to reduce the unnecessary friction that enters into the supplying of our necessities. Develop whatever is at hand, which you know serves your purpose: in this way you will come to a task that becomes even lighter. Cease hankering after the hypothetical and the untried, that is, if this means your apathy and destruction of what is known to have some good in it: for remember that tuberculosis has always shown itself to be almost uncanny in its grasp of actual conditions and opportunities.

There are not a few men who have been so impressed by the decline of tuberculosis, which parallels *in time* the birth and development of our industrial era with its marvelous expansion of wealth and comforts, that they will allow nothing to intentional efforts to reduce the inroads of tuberculosis. It is only fair to say that mathematically we can no more refute them than they can prove their point: and, since they cannot prove it, it would seem little to our purpose to attempt a refutation. Yet it does seem curious that our larger life insurance companies which can have not even a sentimental interest in the organized tuberculosis movement, provided we have merely been beating the air, are continually calling attention to the reduction in mortality *that has been brought about by organized endeavor*. I leave the mathematical calculation of spatial relations to their own trained statisticians, with more confidence than I would have in my own ability to interpret the meaning of figures or in that of our sceptics.

At the moment a chart of the death rate from tuberculosis in New York City lies before me. It shows that in 1900 the total death rate was 280, made up of a rate of 237 for pulmonary tuberculosis and 43 for other forms. I think it will be conceded by all that, in the twenty years that have elapsed since our pre-National Association days of 1900, we have made some progress in diagnosing tuberculosis and a marked advance in reporting deaths from it. There are to-day not nearly the ignorance and concealment of tuberculosis as a cause of death that existed then. Yet the chart shows a total mortality rate of 126 for

1920, the resultant of 109 for pulmonary disease and 17 for other forms. It is simply unbelievable that so remarkable a decline represents merely the reflection of social and economic betterment on tuberculosis—through a period which suffered a war, several years of unusual pneumonia mortality and an unexampled scourge of influenza.

Without our sceptics and apostles of negation we would no doubt lapse into flabbiness, smugness and inertia. We should welcome them; yet we must always insist that they prove their case, for I cannot recall a single important measure, undertaken by the organized antituberculosis movement, which was not based on the best scientific information available at the time. It is all very well for the man with mind centered on the biology of the germ to tell us that we are all wrong. It is his privilege; but he must have something better than dreams and speculations to make us turn from due and proper attention of the victims of the germ. It is again within everybody's province to toss off a sweeping condemnation of sanatoria as places for the relief of tuberculosis: we might even aid and comfort him with statistics, got up in a certain fashion. But we must ask whether he understand the functions of sanatoria and whether their limitations are inherent or merely phases of a situation which society has neglected to meet and which are beyond the control of the sanatoria.

I mention sanatoria advisedly, for the reason that I find myself reading more and more about their uselessness. Now, anyone with a taste for numerical literature and hardened in the reading of sanatorium reports, will soon appreciate two outstanding facts about sanatorium patients. The first is that they do extraordinarily well while in sanatoria. The second is that, after about twenty years after they have left the institutions, most of them have died of tuberculosis.

To me this combination of circumstances proves only two things, namely, that sanatoria are excellent places for consumptives and that the world outside of them is the very reverse. It indicates, moreover, that if we had more sanatoria, enough to keep patients for a much longer period than the customary six months of residence, many more would survive the shocks of everyday life to which they return. For the last twenty years no one familiar with sanatoria has imagined that the ordinary patient, obliged to return to home environment and in many cases contribute to family support, can be "cured" of tuberculosis with even the remote expectation that he stay "cured." Few would venture the opinion that a well managed sanatorium ever harmed a consumptive;

but there are thousands of former consumptives who would testify that sanatoria had saved their lives, thousands who experienced a return to health during their stay in the institutions and who, favorably situated afterwards, avoided relapse by following out the precepts learned in them.

That many, perhaps most, sanatorium patients ultimately die of tuberculosis is no fault of the institutions or the principle that brought them into being. It signalizes a gap, and 'an important one, in our present methods of solving the tuberculosis problem. It points out the need of some helping hand, some adjuvant, for discharged patients to help them over the rough places and make easier for them those three or five most critical years that follow a first arrest of clinical tuberculosis. That Doctor Pattison of the central office of the National Association is at present working out plans to meet this need, as reported in the August *Bulletin of the National Tuberculosis Association*, is one of the most heartening pieces of news that we have had in several years. Better care and supervision of old patients is a situation which must be met and will be met. Its returns will be large: a reduced ultimate mortality, more complete records and control of our vast shifting tuberculous population and many more returned to industry will surely result.

We have thus far touched upon diagnosis, the development of phthisis, the reduction of mortality, the prevention of infection, sanatorium treatment, and the supervision and rehabilitation of arrested and treated cases as elements of our tuberculous problem. The reduction of mortality, the development of phthisis, the prevention of infection and the rehabilitation of treated cases present the major complexes for solution. Of these the reduction of mortality is perhaps the most important, because it is at any time the most immediate and pressing problem, involving, as it does, the care and treatment of the positively tuberculous.

We attack the problem of mortality from several angles. We aim to restore to health those who have fallen ill; and here enter our problems of treatment. We know to a certainty that the earlier a case of active tuberculosis is detected, the greater are its chances of arrest and cure: here crop up our problems of diagnosis, of medical education and of bringing home to the lay public the possible significance of the more common symptoms of tuberculosis, for the all too frequent failure to start patients early enough on the road to treatment is due quite as much to their own disregard and neglect of first warning signs as to the ignorance and slackness of physicians. Most deaths from phthisis occur, not at the end of a continuous illness, but after a protracted up and down course of alternating periods of comparative well being and relapse: the solution of our problems of so called after-care and of adjusting the consumptive to his environment is, therefore, bound to be as necessary as any, and I am confident that it will be worked out. Since there would be fewer deaths if fewer people fell ill with tuberculosis, the problem of mortality is intimately related to and dependent upon that of the development of phthisis.

I should say that at present the last named major problem, that of the development of phthisis, ranks second only to that of mortality. Broadly speaking, it should take first place, for it is the heart and kernel of the whole tuberculosis situation. We can certainly reduce our death rate most effectively and economically by preventing illness. I imagine that if we would have accurate and adequate records before us, we would find that the proportion of mortality reduction brought about during the last half-century through the broad influence of social and economic changes has depended largely on the fact that fewer people are falling ill with tuberculosis. Several men, now well along toward seventy, have mentioned to me that it is their impression that consumption is not nearly the common disease it was when they were younger. Allowing for errors of diagnosis and the contracting circle of friendships and acquaintanceships of advancing age, it is nevertheless probably true that consumption,—advanced pulmonary tuberculosis,—has undergone a notable reduction of incidence.

The problem of the development of phthisis is our most complex one, and goes deep—deep into our most involved knowledge of pathology, infection, resistance and heredity, and deep down and through our social and economic structure and the habits, customs and activities of man. It cannot here be gone into with any detail: and only a few observations must suffice.

The occasionally expressed opinion that there has been less tuberculosis or more benign forms of it during the last hundred years, because during this period universal infection has been bringing about the natural immunization of human beings will hardly bear serious analysis. As a major cause of death and illness tuberculosis has been taking its toll for thousands of years. The situation as regards infection in cities, in homes where consumption existed, and in ordinary traffic and intercourse must always have been worse than it is to-day. For centuries tuberculosis had apparently maintained a level of "saturation" throughout Europe, and began its noticeable decline with the dawn of the universal lightening of man's labor by machinery and a consequent enormously accelerated multiplication of wealth. There can be no doubt that infection confers a measure of specific immunity; but it is difficult to understand why this immunity has been operating through only the last fifty or a hundred years. As a matter of fact, the major part of the people of Europe must have been infected and as immune as they are to-day for centuries. In 1913 the inhabitants of Europe were surely as immune as they were in 1910 or are to-day; but along came a war and active tuberculosis increased by leaps and bounds, to levels that had not been recorded for decades. Wherever the sum total of prolonged stress and deprivation was greatest, there tuberculosis made its greatest gains. This fact will serve to give us some insight into what brings on tuberculosis and what stays its hand.

This phase of the tuberculosis problem and public hygiene are peculiarly interdependent. Both are advanced by ceaseless effort to better conditions under which we live and work, and by educational propaganda. Slow and long continued medical observation of delicate school children and special schools adapted to their physical needs are bound to prevent the outbreak of many cases of tuberculosis in both childhood and adult life, as well as nip in the bud many others which may be developing. The popular education of children in tuberculosis and public health and the organizing of them into "health clubs" have only lately begun. Both cannot help having a decidedly salutary effect. It is safe to say that, where one child knew something about tuberculosis ten years ago, a hundred do so now. But it is not in personal application where we must expect the greatest effect: it is in familiarizing coming generations with tuberculosis and its results, in such measure that the citizens of the future, with sympathies and interest long before awakened and maintained, will be all the more accessible in giving their support to the warfare against tuberculosis. No matter how slight or vague may be the immediately direct and apparent results, we should keep at this education of the children incessantly.

Were every physician alive to the contributory effects of many other diseases in bringing on tuberculosis, and the conservative and special therapeutic measures to be taken in the circumstances, many cases of frank tuberculosis would undoubtedly be prevented. Similar appreciation of the masked and minor manifestations of tuberculosis, particularly in children, would avert many a later catastrophe of more serious disease. It is here again, therefore, that the proper education of physicians and medical students enters into the problem.

There is scarcely any doubt that in a certain number of cases the development of phthisis hinges on unusual exposure to infection—either wholly or in part. The primal problem of the prevention of infection loses, in consequence, none of its point, even though newer concepts of infection and disease have latterly altered our views of the prevention of infection considerably.

We no longer regard *ordinary* natural infection as a determining factor in producing manifest disease: indeed, there are some who hold that ordinary infection is a safeguard. At any rate, most natural infections are so slight or are of such a character as never to inconvenience us in the least. Notwithstanding this benignity, it would be surely our duty to prevent all infection, if we could. But the naked fact is that at present the distribution of tubercle bacilli enjoys such a wide range that we cannot. It is common experience to obtain positive infection tests in people, in young children, for whom the slightest and most transitory contact with bacilli cannot be established: and we have no other recourse than to assume that viable germs lurk in the most unexpected and out-of-the-way places.

Now, most of these must come from some spitting or coughing consumptive. And every consumptive trained or "policed" into the proper disposal of his sputum lessens the sources of infection by just so much. We should, therefore, become more militant in our antispitting campaign and arouse a more or less complacent public to its enforcement.

As to the danger from the careless consumptive who insists on grossly infecting his environment, and as to the measures to be taken to minimize it, there can be no two opinions. Such a man becomes, by virtue of every consideration of public safety, a case for the police. My own general point of view is such that I would probably be the last man to invoke too readily the enactment of legislation or the arm of the law to solve our health problems. I believe that popular education and sympathetic persuasion will in the long run accomplish more, and this in shorter time. But it will usually be found that the thoroughly refractory consumptive has something of the imbecilic or vicious about him which may yield only to force.

But by far the greater number of consumptives' [illegible]s need the light of sympathetic instruction, not the tug of the strong arm. And, throughout the world, one of the most effect[illegible]tituberculosis measures, once it is properly developed, will be h[illegible]nstruction, on the basis of a case of infectious tuberculosis in the house, which will follow in the wake of the reporting of the case to the public authorities. Once reporting is thorough and complete,—[illegible] this will mean still more education of physicians,—and once e[illegible]ty has an adequate staff of home visitors, of the right sort, wh[illegible] function is to extend aid and to inspect and instruct, our morbidity and mortality declines will in time become still more marked than they have been.

Solving tuberculosis in any community means, of course, that we proceed effectively along all lines. To emphasize one while we neglect another may be merely to balance factors, or like adding pluses and minuses. Some localities have developed one or several plans of attack to an unusually high degree and, in particular respects, have furnished us with models; but no one community has tasted of the rewards that would follow a completely rounded campaign based on our present knowledge of tuberculosis.

During this recital it must have occurred to you more than once that the bases of our attack on tuberculosis are all broad facts and generalizations gathered from medical observation and research. And it may be ventured that, granted that our information is correctly applied, we will approach the final solution of tuberculosis problems as we advance in our knowledge of the nature of the disease and its effects. In fact, the only basis which any intelligent tuberculosis campaign may have is one grounded on medical science.

It follows, therefore, that underneath all our efforts to fight tuberculosis must be the most active spirit of study and discovery. This and its results, and these alone, will ultimately solve tuberculosis. If society is to make notable progress against tuberculosis it must encourage research in it. The marvel to-day is not so much the vast body of information that has been accumulated, as the fact that this has been done with meagre resources. We can only hope that the future will disclose more generous provision for the pure study of tuberculosis; for it deserves lavish backing, both on the score of the magnitude of the problem and on the record of past performance of investigators of the disease. We must have permanent foundations, affiliated with teaching hospitals, which, in addition to ample facilities for experimental work, will enjoy the advantages of a wealth of clinical material, will be in a position to instruct both medical student and physician, and, most important of all, can offer careers of sufficient influence and dignity to attract the most promising of our young graduates. Make tuberculosis a major subject of medical teaching and study, and superior men will flock to the field.

Hardly less important are the interpretation and orientation of our knowledge and its dissemination. We need more critics and commentators—bookkeepers, as I said before—men of the broadest experience and knowledge and vision who will give of themselves to the cause. Nothing will continually enliven interest in tuberculosis quite so much as intelligent discussion. We need also compilations and digests of all related published work, and easily used reference indices, available to all serious writers and teachers on the subject. All this has been appreciated by the authorities of the National Association, to an extent that it has provided with unusual liberality for a beginning along these lines.

Then there is the machinery of the warfare on tuberculosis. We can dig out the ore and sometimes fashion the tools, but you, the tuberculosis apostles who work among the public, must adapt them and erect the machinery to apply to the task. When applied to matters that merge so intimately into human relations as tuberculosis, the word machinery strikes a chord that sends out a repellent timbre. Nevertheless, something like it is necessary in our effort at solution, whether we call it machinery, plan, scheme, organization, or what not. No matter how high-minded our intentions or how profound our understanding of the situation may be, we become effective only as we proceed with well matured—and, may I say, elastic—system. I venture "elastic" because, as I conceive it, the tuberculosis situation is bound to differ in detail in every community; and in every place well tested methods must be modified and moulded to the actual local conditions: besides, I sometimes get the impression from what I read that antituberculosis measures are in some quarters looked upon as rigid and immutable methods of procedure. Again, as in every other human pasture, so in the intensely human one of tuberculosis work, personality counts vastly more than technique; and this is the first lesson that the field worker, who wishes to help to solve and not to complicate further a supremely difficult problem, should take to heart.

I haven't a very exact idea of why I was asked t[illegible]ak to you on my particular topic. I cannot persuade myself that [illegible] executive officer looked to me to tell you anything new about th[illegible]erculosis problem. The organized tuberculosis movement in this c[illegible]y has been so alert and responsive to the significance of everyt[illegible]that may relate to tuberculosis or contribute to its conquest, that [illegible] years of unrelenting work, it may now fairly be said to have vulgarized and popularized the subject. It has surely brought home to y[illegible]ong ago—every phase of the problem which I have touched upon and every key to its solution—and much more besides.

I have therefore not tried to tell you anything new; for, to be truthful, I cannot. But, even though all of us agree on the nature of the many elements that might enter into the formation of a highly complicated whole, every one of us, if we are honest, will undoubtedly view the relationships existing between the several elements, and between these and the whole, through different lenses: we will weigh them on balances which will vary in scale: for we see through the eyes of our individual experiences and score our ponderables accordingly. I have therefore thought it best to restate the problem, and, more or less at random, and in detached fashion, set before you to-day's views, based on the trend of tuberculosis work of the past, and likely to change to-morrow with any readjustment which new contributions may make necessary.

Yet, there is one central thought concerning tuberculosis which I think will stay with me through whatever changes which the future may evolve in my point of view. This is that tuberculosis is not an isolated phenomenon in human existence, to be regarded solely by itself: we must come to appreciate its relationships with all human affairs and its interactions with these. And, if you will apply to tuberculosis what I am about to quote, you may understand better what I mean. In an editorial on a subject remote from tuberculosis, I recently read in *The Manchester Guardian* as follows:

> The theory of the web of life is the keynote of modern natural history, and we are always gathering new instances of infinite and unexpected connections. To kill a wagtail may be to bring disease to a flock of sheep. Who drives out bees drives flowers from his land. In exactly the same way social reform is distorted by rigid analysis. The problems of society merge in a single complex of moral and economic adjustments. By building houses we empty hospitals; prosperity slackens the pressure on the prison; schools and schooling tilt the balance against the police court.

NOTES ON THE ANTITUBERCULOSIS CAMPAIGN IN THE WEST RIDING OF YORKSHIRE, ENGLAND

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There is so much in common in the efforts which are being made by America and Great Britain in combating tuberculosis, that it may savor of redundancy to go into details of the work which is being carried on in the West Riding of Yorkshire, England.

Yet there are certain differences between the schemes of the two nations which may prove of interest to members of the profession engaged in the administration of tuberculosis schemes in America. To enumerate the details without stating the essentials of the campaign as a whole would, however, not do justice to the efforts which are being made throughout Great Britain.

Before dealing with the work in the West Riding it will be well therefore to point out one difference, not of detail, but of fundamental importance, in the antituberculosis campaign as it is carried out in this country.

THE MINISTRY OF HEALTH

The Ministry of Health has, as its chief function in tuberculosis, the levelling up of the schemes of the various local authorities. No expenditure of any kind can be undertaken without the permission of the Ministry, and even appointments to the tuberculosis staff of any local authority are subject to the formal approval of the Minister of Health. The government grant in respect of institutional treatment alone is 50 per cent of the total expenditure, while the dispensary system, and the other units in the scheme, for instance, the medical and nursing services, are also subsidized from government funds. It will be seen therefore that practically every detail concerning the financial aspect of the question is under the Ministry's control and subject to their approval. It must not be thought that local progress is hindered by what may appear at first sight to be government restriction: on the contrary, the desire and aspirations of the Ministry are so high in many things that it is only by great effort that local authorities can keep constantly abreast of the exacting demands imposed upon them from London.

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Not the least important function of the Ministry is the setting up of special committees to investigate questions of particular interest at a given time. The findings of these committees are printed and distributed to tuberculosis officers in the country, who have, if they choose, an opportunity of discussing the details as they affect each area with the Ministry's medical adviser. The network of training colonies for tuberculous ex-servicemen is a product of the deliberations of one of the special committees referred to above.

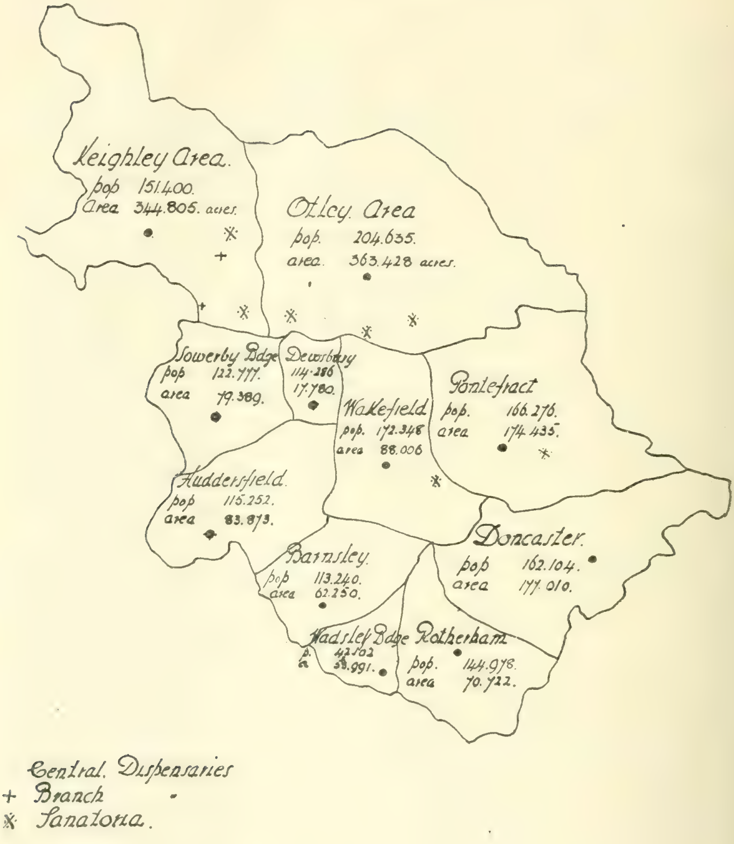
The Ministry of Health is always prepared to receive and consider suggestions from tuberculosis officers attached to local authorities, and experience has shown that these suggestions have occasionally been acted upon by the Ministry to the benefit of all concerned.

Following the example of the Ministry itself, each local authority,—county council or county borough as the case may be,—has its own tuberculosis department, and, with a few exceptions, its own tuberculosis medical staff, composed of men specially trained in the diagnosis and treatment of the disease.

The Medical Officer of Health of the county or county borough is Chief Tuberculosis Officer, but in the larger areas the great bulk of the work falls upon an assistant who has been appointed Tuberculosis Officer, and who is, or should be, a clinician as well as an administrator. For many years past there has been much difference of opinion as to whether the Tuberculosis Officer should be a clinician first and an administrator next, or vice versa. Whatever the more desirable combination may be, there can be no doubt that a man who is merely a clinician does not make an ideal Tuberculosis Officer. In urging all officers to take a keener interest in the preventive side of the question the Ministry of Health is making a recommendation which has much to support it from past experience.

THE WEST RIDING OF YORKSHIRE SCHEME

In placing the West Riding Scheme before readers of the AMERICAN REVIEW OF TUBERCULOSIS, it will be well at the outset to say that the area covered by the administrative county is approximately 1,640,000 acres, that is, 2,400 square miles. The population is estimated at



Map of the West Riding of Yorkshire showing the Dispensary Areas, Sanatoria with the population, acreage, of each area

June. 1921.

1,492,592 (1920). A more complete mental picture of our county may be given to American readers if it be said that, so far as population and area are concerned, the West Riding Administrative Area would be reproduced in the United States if the entire population of South Carolina were transferred to the State of Delaware.

As a local authority, the West Riding has the largest area in England, but the population is only the third largest in the country.

The County Medical Officer is Chief Tuberculosis Officer. Since 1913, however, there has been a special staff appointed to deal with tuberculosis as distinct from the other aspects of public health. This staff is composed of a Chief Clinical Tuberculosis Officer, 11 district officers, and 20 specially trained tuberculosis dispensary nurses, who are reinforced in the districts by 60 Health Visitors, who incorporate tuberculosis visiting with the other branches of their work.

The Chief Clinical Tuberculosis Officer has his offices and clerical staff at Wakefield, which is the centre for the administration of all County Council Departments (see map). Here he is in direct touch with the County Medical Officer of Health, with whom he may consult on problems which encroach upon other departments of the public health service, and from whom he may obtain advice on important administrative matters. As can be readily understood, there are so many questions which border on the clinical and administrative aspects, that to define the Chief Clinical Tuberculosis Officer's duties entirely in the terms of his official designation would be to leave many most important details in "no man's land."

But whatever the difficulties may be in other areas in differentiating administrative from clinical duties, there is none in the West Riding, and in no instance has dual control ever been responsible for what may be termed, for want of a better name, "official bungling."

The Chief Clinical Tuberculosis Officer is entrusted with the general supervision of the Council's scheme. He reports to the Public Health Committee at monthly intervals on all cases admitted to and discharged from sanatoria and hospitals, as well as on cases attending the various dispensaries. All recommendations for treatment, whether for sanatorium, hospital, dispensary or domiciliary, are submitted to him for approval by the District Tuberculosis Officers, and, in cases where institutional treatment is recommended, admissions are regulated direct from his office.

It is his duty also to keep the District Officers informed of new and important alterations in procedure, as may be decided upon from time to time by the Ministry; in addition, he has to keep careful records of, and act up to, the resolutions passed by his Committee.

It not infrequently happens that special reports are asked for by enthusiastic and well-meaning lay members of the Public Health Committee on matters concerning sanatorium returns, incidence of disease in certain localities, the minimum requirements for institutional treatment of nonpulmonary tuberculosis, etc. Such reports are compiled by the Chief Clinical Officer and distributed to all members of the committee prior to the next meeting. One feels that such work is well worth while even if one is compelled to condense important data, and deprive it of explanatory medical terms in order to make it readable for laymen. When special reports are considered to be of special value, they may be printed and circulated to all members of the county council, and to others who may be interested in the work of the Public Health Department. As a means of local propaganda, this course has proved useful on more than one occasion.

Perhaps the most exacting part of the Chief Clinical Tuberculosis Officer's work is to prepare and keep within the estimates of expenditure for the financial year. The expenditure per annum on tuberculosis in the West Riding is at present about £120,000. Every item must be detailed, even to the amount to be expended on oil-canvas for the domiciliary shelters. The task of keeping a close watch on each and every item in the annual budget is no easy one, but where and when possible a monthly report is prepared showing the rate of current expenditure under the various heads.

It comes as a pleasant relief to the Chief Clinical Officer to undertake the essentially clinical part of the work, for which he was, after all, more particularly trained. And for the keen clinician there is much to do. His visits to sanatoria and hospitals are not so much for the purpose of examining individual patients as for taking a bird's eye view of the working of the institution from both the clinical and administrative standpoints. He may of course consult with the medical superintendent on particular cases admitted from the districts, or he may have the much more unpleasant duty to perform of bringing to the notice of the resident authorities complaints made by patients. In this branch of the work, the greatest possible tact is essential, for just as the methods of administration of sanatoria and hospitals vary, so do medical superintendents differ in temperament. Still, the task of investigating complaints must be done, but in the West Riding these are not common, and consequently the visits to the institutions are among the more happy experiences of the Chief Clinical Officer.

The supervision of the dispensaries and interviewing of the district tuberculosis officers are also included in the Chief Officer's programme. It is found that personal interviews accomplish infinitely more than correspondence by post, and that many points which cannot be approached conveniently on paper may be brought to the notice of the Chief Clinical Officer by the District Tuberculosis Officer, who is in possession of first hand knowledge of local conditions. No new branch dispensary, for instance, is ever opened without taking the views of the District Officer into consideration, and a tour of inspection of the locality in the company of the District Officer is a procedure adopted by the Chief Tuberculosis Officer in every case where a request is made for the establishment of new premises.

Every new item which involves financial outlay, however small, is reported to the Public Health Committee at the monthly meetings, but the more thorough the preparation of estimates at the beginning of the financial year, the less should be the need for coming before the committee at any time during the year for special grants for new ventures.

An endeavor has been made to hold conferences of district tuberculosis officers at Wakefield at least twice a year. Two or three questions of special interest are introduced and discussed, but an additional advantage of these meetings is that the social side of the service is developed. It is realized that for uniformity of work there should be, as far as possible, uniformity of opinion on medical matters, but it is also true that much is to be gained by a free interchange of ideas on nonmedical matters between officers who are working together in the same service under the same local authority.

Statistical tables, setting out details of attendances, diagnosis, deaths, expenditure on drugs and appliances at the various dispensaries, etc., are compiled by the clerical staff at Wakefield and issued at intervals to the district tuberculosis officers, who may in this way have some idea of the extent and scope of the work in other dispensary areas in the West Riding. The time and trouble taken in this important branch of the work is, I believe, well spent.

THE SUBDIVISION OF THE COUNTY INTO AREAS FOR TUBERCULOSIS ADMINISTRATION

For purposes of tuberculosis administration, the West Riding is divided into ten sections (see map); each section being composed of a number of sanitary districts. As will be seen from the map, the acreage and population of these sections or areas vary, but, with the exception of the Otley area, which is too large, there are geographical and other considerations which render this subdivision of the county into ten areas a most convenient one. It is always difficult to determine the exact amount of work which should be allocated to each full time tuberculosis officer. In a report issued recently by the London County Council, it was estimated that no officer should deal with an area in which more than 160 deaths from tuberculosis occur per annum. This figure, when applied to the West Riding Dispensary Areas, is too large, for many of the districts in the Riding are essentially rural. As a matter of fact, each District Tuberculosis Officer has approximately 100 deaths per annum in his area,—again with the exception of the Otley District which, as already mentioned, covers too large an area.

The different dispensary areas vary greatly in physical features, and in the manufactures which give employment to the population. Briefly, it may be said that the western and northern portions are hilly, while the eastern and southern districts are flat. Some of the townships on the Pennine Range are over 1000 feet above sea level, but the flat land near Goole and Doncaster is actually at the level of the sea. The geology of the county likewise presents peculiar differences in places. On the west there is a distinct band of the Peruvian system made up of marl and limestone, running the whole length from north to south. Near Skipton are the grits, but in the central and southern districts are the coal measures on which the towns of Wakefield, Barnsley, Rotherham, Doncaster and part of Sheffield appear.

Manufactures. The West Riding of Yorkshire is noted for the variety and quantity of its exports. It would be out of place to record here in any detail the distribution of the various manufactures carried out in the county, but it may be said briefly that coal mining is confined to the central part, the south and the southeast; textile manufactures to the west; and agriculture to the north and east. The "midlands" of the Riding, as represented by places like Leeds, Keighley and Wakefield, show a greater diversity in industry than is found in any other district in the county, for here we have mining, textile work, glass making, and engineering as means of employment for large numbers of the population.

It is not surprising, therefore, in view of the marked variation to be found in different parts of the county, that the work of the district tuberculosis officers should be of great interest when collected and subjected to careful analysis. At the present time, the same dispensary routine is in operation throughout all the areas shown on the map, but from evidence which is gradually accumulating, it is becoming more and more apparent that our efforts to combat the disease will require to undergo certain modifications in the light of statistical results. This will be referred to later on.

Each Dispensary Area is under the direct control of the District Officer, who resides in the area. There are one central and one or more branch dispensaries in each area, all situated at convenient geographical points to suit the needs of the population. The clinical work of the dispensaries is on the usual lines. The original function of the dispensary as a diagnostic centre is constantly borne in mind, and treatment, *except in special directions* (for instance, tuberculin and artificial pneumothorax therapy, the "brass" treatment of lupus, and the modern methods applied to nonpulmonary tuberculosis cases), is not encouraged. Attendances are large, especially at the central dispensaries, where as many as fifty patients may attend during a session. We have found in certain areas that the setting apart of special sessions for special cases, for instance, Saturday mornings for children, evenings for workers, etc., has helped the organization of the work very considerably.

The District Tuberculosis Officer is empowered to pay the travelling expenses of patients who may reside at some distance from the dispensary, but only in cases considered by him, after investigation, to be necessitous.

A most important aspect of this work in the districts is the home visitation of cases. This is conducted by the officers and a staff of nurses. Of the 82 nurses engaged in tuberculosis visiting, 20 are specially appointed as Dispensary Nurses, and they are always in attendance at the dispensaries with the tuberculosis officers, to assist in the taking of records, temperatures, weights, etc. Their whole time is devoted to the tuberculosis side of the health service.

Weekly reports of the work done by each dispensary are forwarded to the Chief Clinical Tuberculosis Officer at Wakefield who is in a position to frame his monthly and annual reports on the information so provided.

In practice, it is found that the system of centralization of recommendations and records works very satisfactorily, but, all the same, one would wish most heartily for a diminution in the amount of actual clerical work to be performed by the district tuberculosis officers, so as to enable them to devote more time to the actual clinical and administration duties which are much more important. Research at dispensaries by individual officers is quite out of the question; this is probably the most unsatisfactory feature of the tuberculosis movement in this country.

The extra work thrown upon the Tuberculosis Department by the Ministryof Pensions (acting in conjunction with the Ministry of Health) has hampered the routine work of the dispensaries in every direction. As it is, the district tuberculosis officers are certainly not in touch with more than sixty per cent of the tuberculous population. One is almost afraid to contemplate what would become of numerous documents of the Pensions Department if every case of tuberculous disease attended the dispensaries.

SANATORIA AND HOSPITALS

When the West Riding County Council's scheme for the treatment of tuberculosis was formulated in 1912, sanatorium treatment was given due consideration. Temporary buildings were occupied at first at convenient places in the county, but progress was made almost at once with the erection of Middleton-in-Wharfedale Sanatorium. This institution is situated on the high land overlooking the River Wharfe, and is within easy reach of the delightful health resort, Ilkley (see figure 1).

The accommodation at Middleton at present is 300 beds, all of which are reserved for male patients suffering from the disease in its early stages. Fifty beds are set apart for patients, mostly ex-servicemen, who are recommended for concurrent treatment and industrial training. This industrial colony at Middleton is one of several in England, built and maintained almost entirely by the Ministry of Health. The original recommendation of the Interdepartmental Committee was that there should be, in addition to training colonies, village settlements on the lines of the now famous "Papworth Industries" in Cambridgeshire, but such a scheme would entail an expenditure far beyond the financial resources of the Ministry. And so it is that each local authority has been left to work out its own salvation in the matter of aftercare for the patients who have passed through the sanatorium and training colony. The Public Health Committee of the West Riding County Council has realized that aftercare is the crux of the whole problem, and has submitted a scheme to the Ministry of Health. The West Riding Scheme, which has not at the moment of writing received official approval from the Ministry, centres around the training colony at Middleton on the one hand and the large Stores Department of the County Council on the other.

FIG. 1. BIRD'S EYE VIEW OF MIDDLETON-IN-WHARFEDALE SANATORIUM, ILKLEY, ENGLAND

It is proposed that general woodwork, rural industries, and poultry farming be the three occupations taught at the colony, and that in the case of the first two trades all orders should be sent from the Central Stores Department at Wakefield to the instructor at the Colony. (The Stores Department is the main source of supply to the hospitals, asylums, schools, and other institutions throughout the county.) The patients at the colony wlll receive an intensive course of instruction to enable them to carry out the less complicated details of cabinet making and boot repairing. When considered by the instructor to be efficient workmen, and when they show signs of arrested disease in the chest, they will be discharged from the colony to their homes, where they will still carry on the work in which they have become proficient. It is proposed that sleeping shelters and small portable workshops, built specially for the county council according to the plan submitted, be supplied to each trainée on his discharge from the Colony. On their return home to their shelters and workshops, the trainées will continue to carry out work for the training colony at Middleton and will receive periodical visits from one of the instructors from the training colony, who will suggest improvements in technique, or point out obvious deficiencies in workmanship should such exist.

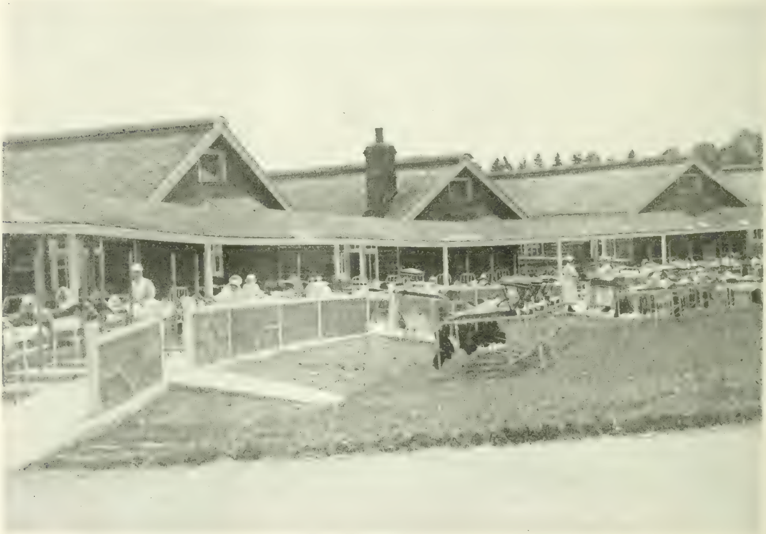


Fig. 2. Lord Mayor Treloar Cripples' Hospital and College, Hampshire[2]

While at the training colony, patients will receive no payment for work done, for they are, after all, still patients, but after their discharge from the colony, payment will be made in respect of actual work done.

It is estimated that the cost of providing a trainée with a sleeping shelter, workshop and tools will be approximately £60 to £70. Such profits as may accrue from the material made at, and exported from, the training colony may be utilized in helping to provide suitable trainées with shelters, workshops, and tools. Should the successful trainée be fortunate enough to develop a local market for his goods through his own ability and enterprise, good and well; but he need never fear of being without work should a local market be unprocurable.

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[2] The author is indebted to Sir Henry Gauvain for the use of figures 1 and 2.

It is to be remembered that a large percentage of the men admitted to and discharged from the training colony will be ex-soldiers who are also in receipt of state pension; this is a most important consideration for men who will never be able to resume their places under ordinary industrial conditions. The great advantages of allowing the patient to live near his own home and relatives, and to work and sleep under the best hygienic conditions possible, are obvious. He has not the feeling that he is undergoing institutional treatment in the ordinary sense, yet he is under the supervision of the District Tuberculosis Officer and the Dispensary staff, who report on his clinical condition from time to time.

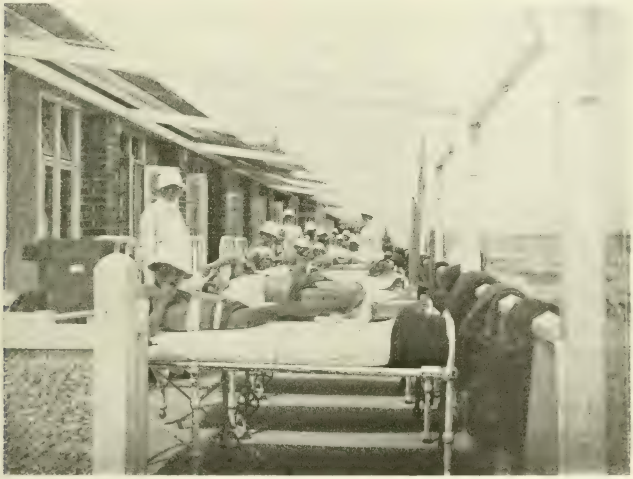

FIG. 3. A PORTION OF THE SOLARIUM, SANDY POINT, HAYLING ISLAND (LORD MAYOR TRELOAR CRIPPLES' HOSPITAL AND COLLEGE)

Middleton-in-Wharfedale Sanatorium will, when the new colony is opened, be one of the largest institutions in England. There are three medical officers in attendance at present, and a staff of 33 nurses, including the matron and sisters.

An X-ray apparatus is installed, and a well equipped laboratory is in constant use by the assistant medical officers working under the direction of the Medical Superintendent. Early cases of pulmonary tuberculosis in males are treated at various other sanatoria in the West Riding (see map) and at institutions outside the Riding, but the county council has no other sanatorium of its own at present on the lines of the Middleton-in-Wharfedale institution. Hospital accommodation in the administrative county is still inadequate for both sexes; only 140 beds are available for acute and open cases. Patients suffering from nonpulmonary forms of tuberculosis are treated at Leasowe Hospital in Cheshire (35 beds), at Thorparch (12 beds) (see map) and at Lord Mayor Treloar's Home at Alton, Hampshire, under Sir Henry Gauvain (20 beds). Little or no difficulty is experienced in getting parents to consent to their children travelling for treatment at Alton, Hampshire, in the south of England, from Yorkshire in the North. Arrangements for the transfer of patients are made by the Chief Clinical Tuberculosis Officer with the dispensary nursing staff and with the Travellers' Aid Society in London, which undertakes full responsibility, and is familar with the intricacies of train, tram and bus service in London and the south.

A survey of the sanatorium and hospital needs of the population of the West Riding has been made quite recently, and 918 beds are considered to be necessary. The county council is negotiating for the use of a large sanatorium to accommodate 300 women and children suffering from pulmonary and nonpulmonary tuberculosis. With the acquisition of these beds the facilities for institutional treatment will have reached the minimum requirements. The waiting list is at the moment a very large one.

DOMICILIARY TREATMENT

There is always a certain number of patients who are unable for one reason or another to attend the dispensaries, and who are not regarded as suitable for institutional treatment. Such cases are recommended domiciliary treatment, and are attended by their private practitioners who have, under the most recent regulations, to render reports on these patients to the District Tuberculosis Officers at not less than three-monthly intervals. But where and when possible, the district officers arrange to discuss cases in consultation with the practitioners in attendance; in this way a very close coöperation arises between the tuberculosis officers and the general practitioners. The inherent dislike for official "interference" on the part of the private doctor is gradually disappearing, and in some areas especially there is evidence that the tuberculosis officers' counsel and advice are taken on every possible opportunity. From experience in different parts of the country one can say unhesitatingly that the success or failure of the domiciliary part of the antituberculosis campaign is an index of the tact and discretion, as well as of the clinical ability, of the tuberculosis officer. The general practitioner does not, as a rule, judge a public health service on the efficiency or otherwise of its administration. He weighs it up in terms of the clinical powers; hence it is of the utmost importance that, to be a real success in his district, the tuberculosis officer must have outstanding clinical ability. It is probably a realization of this principle that has led the tuberculosis officer to neglect in some measure the numerous administrative duties which also fall to his lot. As an ancillary part of domiciliary treatment, mention may be made of the sleeping shelters. There are 100 of these distributed throughout the county, at or near houses in which there are poor facilities for the observance of the fundamentals of open-air treatment. Special funds are also available for the provision of extra nourishment for patients. With the recommendation for extra nourishment for tuberculous ex-service men the local authority has nothing to do, but as there is only a sum of £3000 (that is, on a basis of £2 per 1000 of the population) available for non-service men, women and children, the distribution of this benefit has to be regulated very carefully. Recommendations for extra nourishment in necessitous cases come from the district officers to the Chief Officer who arranges directly with the merchants for the supply of goods—usually milk and eggs. Approximately, 240 patients are receiving extra nourishment in this form every week.

MORTALITY RATES AND EPIDEMIOLOGY OF THE DISEASE

It has been said that the criterion by which a large public health measure should be judged should be the mortality rate. Analogy with typhus fever, typhoid fever, malaria, and smallpox would seem to bear this out, and if one looks at the mortality curves for tuberculosis in the West Riding there would appear to be some evidence that the campaign in this country is meeting with undoubted success (see chart).

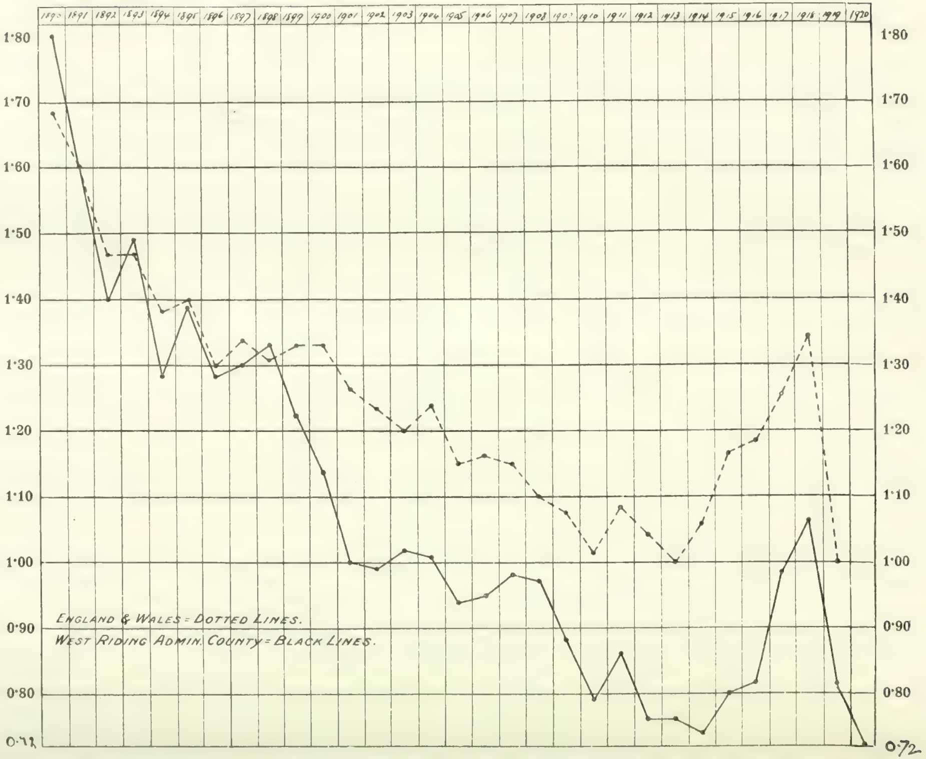

Chart 1. Showing Death Rate per Thousand from Pulmonary Tuberculosis for the Thirty-One Years in the West Riding Administrative County as Compared With England and Wales

The most optimistic and enthusiastic worker in tuberculosis cannot, however, look at the results of the fight, and pretend that anything approaching a complete mastery over the enemy has been achieved. The opinion and proofs of more recent writers of authority have confounded many of our cherished beliefs; so much is this so, that we would be rash indeed if we reconciled ourselves to the fact that by adopting a policy of *laissez faire* we are doing our utmost to attain our aim and object. Just as we look to the Ministry of Health to give guidance and sense of direction to our administrative efforts, so also must we follow up and explore the paths laid open for us by men who have discovered large avenues fertile with astute clinical observations.

In taking up the thesis of Brownlee that phthisis is not a single disease, but a mixture of several types varying according to age and locality, the problem of local incidence in the West Riding was approached with a view to ascertaining whether there might possibly be variations in the type of the disease within the confines of the county itself.

To embark upon such an investigation, one is required to have reliable statistics of mortality rates in the various sanitary areas, details of ages and death, coupled more or less with an intimate knowledge of the geographical, geological and other features of the county. The task of enquiring into this subject has taken many months, but from the findings one is able to say definitely that although the mortality rate from phthisis has decreased in the West Riding Administrative Area, yet *in certain areas* there has been practically no improvement in the death rate from the disease.

As Brownlee has pointed out, (and our investigations support his conclusion) the prevailing type of phthisis in the West Riding of Yorkshire is the middle-age type. But although this is so, there is a difference in the mortality rates from the disease in different age groups in the various dispensary areas in the county. For example, the death rates from pulmonary tuberculosis (and from other respiratory diseases) are two to four times greater among children under fifteen years of age in South Yorkshire, particularly in the Rotherham Area, than in Western Yorkshire, that is, in the Sowerby Bridge and Huddersfield Areas (see map). Our observations tend to show, also, that there is probably a certain amount of acquired immunity to pulmonary disease among adults in the Rotherham Area. It is difficult to explain the reasons for this variation in the mortality rates, among children especially, in districts which are, geographically, practically contiguous, but the one common factor which apparently decides a high infantile and juvenile mortality rate is *atmospheric contamination*, for this is the one feature common to the areas in which such rates are found, that is, in the mining and industrial areas with a low rainfall and situated at a low altitude.

It is a singular fact also that open cases of phthisis are more numerous in the textile centres where a large percentage of the adult population of both sexes spend most of their time in factories and in homes. The textile centres are almost exclusively confined to Western Yorkshire, where the children are remarkably free from tuberculous disease. This fact would point to a lack of immunity in the adult population of these areas, a statement which is supported by Bushnell's views. It must not be forgotten, however, that the nature of the employment of the majority of the population in the West may be, and probably is, an important factor in bringing about massive infection.

These conclusions serve, I believe, as a valuable stepping stone for our future work. They point to the necessity for greater efforts in safeguarding the lives of children in South Yorkshire, where the toll is very great. The urgent need for open-air schools in pure air zones is obvious, and is being strongly advocated. In the western areas we plead for special attention to factory hygiene, by which is meant the routine medical examination of workers and the full observation of the details of ventilation and prevention of infection. Already a systematic survey of the school children in a small township near Rotherham is being undertaken, in conjunction with the school medical inspectors, where the incidence of tuberculous and other respiratory diseases reaches a very high point. The results of this survey are being awaited with interest.

The moral of our findings so far is that the campaign which we are conducting in the west of the county is not adapted to the needs in the south. We shall require to reorganize somewhat in the light of our statistical findings. And what is true in this county is very likely true of every large area. Dr. Brownlee, in a personal communication, advises local research on these and similar lines. No one without intimate knowledge of local conditions is in a position to analyze and explain the mysteries of local mortality rates. We believe that little progress can be made by attacking the enemy uniformly when the opposing forces vary. If our views are substantiated by further clinical observations, a great step forward has been made.

INSTITUTIONAL TREATMENT OF TUBERCULOSIS: ITS LIMITATIONS[1]

A. F. MILLER

Nova Scotia Sanatorium, Kentville, Nova Scotia

For many years it has been my duty to try to popularize and justify the work of a sanatorium, and I hope it may never be said that I have "gone back on" that principle. But it is an undeniable fact that sanatoria—the sanatorium idea and its limitations—have been somewhat disappointing in their results, so far as any appreciable reduction of the death rate from tuberculosis is concerned. This is partly by comparison with the somewhat extravagant hopes entertained when the real value of the open-air and rest treatment became known, and when the good news that consumption is curable by these means raised the spirits of health seekers, and institutions of the sanatorium type sprang up the world over.

This is not by any means to say that excellent work has not been done, nor to forget that many lives have been saved by institutional treatment. But to limit the work of the sanatorium to curing incipient or early adult cases of tuberculosis is to miss a great part of the good that an institution should accomplish. This was necessary some years ago, to prove to the public that tuberculosis could be cured and that institutions for this purpose were justified and worthy of support. Better results could be obtained from early cases, and therefore the pioneer sanatoria admitted only the curable type. Their results served the purpose; to-day the public is convinced and is in a fair way to being educated along these lines. Now there is, indeed there always has been, the demand for admission of advanced cases for treatment. This necessitates a different sort of institution from the sanatorium proper. It means a larger nursing and working staff, because it means facilities for bed-rest in the great majority of cases. In short, the tuberculosis sanatorium of the present day must have in connection with it a hospital, or infirmary, to which all incoming cases can be sent for a longer or shorter period of bed-rest which is now recognized as probably the most important part of "the cure." This infirmary should not be, and cannot be, merely a place for hopeless cases. Its function must also be that of a receiving and distributing centre from which patients are graduated into pavilions according to their progress toward health. This is the system we are attempting to work out at the Nova Scotia Sanatorium. In such a system the patient with far advanced disease does not feel that his last days have come when he is brought to a place where he sees others improving and leaving.

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[1] Read at an open meeting of the Public Health Section of the Canadian Medical Association, Halifax, Nova Scotia, July 6, 1921.

But at its best the institutional treatment of tuberculosis is not entirely satisfactory, so far as permanent results are concerned. The patient spends only a few months under these more or less ideal conditions, whereas tuberculosis in most cases demands a change of living conditions for the whole lifetime of the patient. As we come more and more to recognize this, we understand and accept the heretofore discouraging tendency of our discharged patients to relapse. And we begin to ask, "What can be done to prevent it?"

Let us look for a moment at the figures representing our actual results of treatment at the Nova Scotia Sanatorium. And I assure you that these results are about the same as those of other institutions in all parts of the world.

In a group of 284 ex-service men discharged in 1920, the pulmonary condition was as follows:

Disease arrested	41 or 14.4 per cent
Disease apparently arrested	52 or 18.3 per cent
Disease quiescent	68 or 24.0 per cent
Disease improved	64 or 22.5 per cent
Unimproved	37 or 13.0 per cent
Died	22 or 7.8 per cent

That is to say, 80 per cent were greatly benefited by treatment.

These results are good and gratifying, as immediate results, and in many individual cases. But, ten years after discharge, the proportion of patients well enough to work is, roughly, only fifty per cent. True, this is sufficient fully to justify the existence of the sanatorium, for it can hardly be doubted that few of these survivors would be alive and well, were it not for the treatment and education they received at the institution. And many others had their lives and usefulness prolonged for some years by the same means. The point I wish to emphasize and build upon is that our results, though good, are not what they might be, and ought to be.

First, briefly, what is the cause of all these relapses? It is largely economic. True, there are faults of character and of education and of environment; there are varieties of physical resistance; and there are what may be called accidental factors which help to bring about breakdown in health. But the broad, outstanding cause is just the pressure of life, the need of earning a living and keeping up to the pace set by others less handicapped. The tuberculous are caught in the grind of the great machine which we call our civilization. They find that, to be self-supporting, they must do work for which they are unsuited or they must work longer hours than they are able. They cannot afford a healthful home life. If there is a family to support, the pressure is so much the greater. The inevitable relapse occurs. And what then? What about the months or years during which they are in a far advanced or incurable condition? This is another element in the problem. To it I will refer later. For the moment, I wish to speak about the prevention of relapse. So far as institutional treatment is concerned, it may be said that every effort has been made to prepare the patient, before discharge, for taking up work within his capacity. The method of graduated labor has been well tried out by Dr. Marcus Paterson and others. While patients are carefully selected and medically supervised they can do a good deal of work, but that is an entirely different proposition from getting out and earning a living after discharge. It has not been found that any method of "hardening" the patient while under treatment has been of real value in preventing relapse when he returns to unsupervised living and self-support.

Society as a whole has a vital problem here to face and the medical profession and public health workers must have some ideas, some vision, some leadership to offer.

There are only two courses open. Shall we let the arrested or quiescent tuberculous patient fight it out alone and drift into advanced disease, or shall we help him to keep his health? Apart from ethical and philanthropic considerations, will it pay us to choose the latter course? And if we decide to do so, how shall we go about it?

The Government of Canada, in dealing with tuberculous ex-service men since the Great War, has blazed trails which we shall find useful in following up our work with the whole population. When it was found that these men were relapsing after discharge and continually returning for re-treatment, usually in a much worse condition than that of their previous illness, it was found necessary to pay the discharged sanatorium patient full pension for six months or more, to cover the period of adjustment, so that he need not take up full time work too soon. For various reasons even this has not been effective, and relapses still occur. Then a commission was appointed to look into schemes for aiding the patient after discharge, including what is called "sheltered employment." We have come to think of Dr. Varrier-Jones and Sir German Woodhead, the enthusiastic promoters of a most successful industrial colony for the tuberculous at Papworth, England, as authorities on the subject of sheltered employment. From their experience and from our own observation, as well as from the exhaustive report of Colonel William Hart, our Canadian representative, we believe that a system of sheltered employment, with organized means for providing healthful living conditions is the only effectual way of handling this problem. And if this is true of the ex-service pensioner, it is equally or even more applicable to the great mass of civilian citizens who have developed tuberculosis, most of them during service to their country in quiet, peace time ways, and whose illness and death are a distinct loss to the national life. We are all heartily willing to work and to pay taxes for the good of the returned soldier; we ought to be. But if an equally thorough oversight of the health of all our people is not a patriotic duty, I do not know what is.

There is not time, in a short paper, to go into such points as the selection of trades and occupations for the tuberculous ex-patient, nor to recount what has been done or attempted in the way of sheltered employment. Neither can I discuss the pros and cons of the establishment of a special tuberculosis settlement—a sort of Arcadia where the simple life, regular hours, healthful homes and quiet recreations may be had, whether one is able to earn all these or not; and where part time work would be done under medical supervision. Suffice it to say, that it is of no use whatever to give the classical advice to a consumptive, "Find a light job in the open air." Jobs in the open air, such as farming, gardening, etc., are not "light" if a man must earn a good living at them. And you may be sure that "a light job means light pay and light pay means a gradual descent into poverty, malnutrition and misery." I may venture to add that, unless it is utterly unsuitable, the work he has been used to is the best for the ex-patient to take up, or some allied occupation with which he will feel somewhat familiar, provided it can be carried on under good conditions for easy hours. It is not the work, it is the pace that kills: and, of course, worry and mental strain.

It must be understood that organized sheltered employment cannot be expected to be self-supporting. But we have heard of one, the Altro garment shop in New York, which paid off initial expenses in a year and has since been self-sustaining.

It goes without saying that if a man can work only three or four hours a day, he cannot compete with full time workers in the open labor market, nor can he always earn the comfortable living that his health demands, even in a "sheltered" system. Someone will have to pay the deficit. It would seem to go equally without saying that, from the economic point of view, it is better for a man to earn a partial living and keep well than to earn nothing during a long illness; not to speak of the happiness and self-respect accruing to patients, and the probability of saving their families from disease and poverty.

I may remind you that the yearly death rate in Nova Scotia—and this is only a little higher than the average for all Canada—is 147.9 per 100,000, and that the estimated loss to the Province is two million dollars each year at the very least. This sum would be quite sufficient to carry on a comprehensive tuberculosis program. But the government cannot be expected to meet all of the cost. Our ever generous philanthropic societies and individuals could be counted upon for material and administrative assistance of the finest sort.

The bringing up of children in healthful surroundings and sending them out equipped for full citizenship is in itself a sufficient balance for the money spent on any system of aftercare for the tuberculous.

This brings me to the broader outlook upon the whole problem. Although I have been emphasizing the relapse of sanatorium treated patients as one reason why institutions have failed to reduce appreciably the death rate from tuberculosis, this is only one phase of the real reason. We shall get at the true reason only when we realize that the campaign against tuberculosis is a chain of many links. If one link is weak or missing, we do not get the necessary pull on our objective point. Institutional treatment is only one link in this chain. Follow-up work among discharged patients, including sheltered employment, frequent examination, etc., is a succession of links. But all this attention to the sick is only part of the chain. Other and equally necessary links are those that make for prevention of sickness. And by this I do not mean the prevention of infection. I need not on this occasion go minutely into the subject of infection. An audience like this is well posted in the broad general truths that, in civilized communities, infection by the tubercle bacillus is almost universal and that as a consequence we all enjoy a comparative immunity; that, when infection occurs in infancy or in any individual or race which has not this acquired immunity, rapid and fatal disease is likely to follow. The so called "chronic," curable type of tuberculosis is a result, not of this first infection but of a lowering of the individual resistance, from whatever cause; and if it develops it is usually long years after infection has occurred. The development of tuberculous disease in the adult and older child is a question of general health and vitality. Everything that bears upon the latter bears upon the former. If we are going to strengthen the chain of our endeavor to overcome tuberculosis and supply the missing links, one of the first moves must be to turn some of our attention away from the "germs" we have been chasing or avoiding and turn it toward the promotion of individual and public health.

Do not mistake me. I am not saying that the existence of tubercle bacilli may be ignored. Under certain circumstances, there is danger and there are precautions which must be strictly observed. There is danger in massive infection, such as may occur in continued intimate contact with a careless patient having tubercle bacilli in his secretions. This must always be guarded against, and sanitary methods insisted upon. Even such contact, when proper care is exercised, need not result in dangerous infection. Let no one imagine that I am depreciating the efforts made to overcome, for instance, the spitting habit, which is a menace as well as a nuisance; nor that I am denying the need of cleanliness, fresh air and sunlight, indoors and out, as prime essentials of health. "These ought we to have done and not to leave the other undone."

As I have said, infants, that is, children under two or three years of age, are very susceptible to this disease and should be rigidly guarded from infection. Occurring a year or two later, the mild, slight infections received in the average way of living are comparatively harmless and act as immunization. Indeed such inoculation is practically a necessity, as our civilization exists to-day; and some of our leading physicians have advanced the idea that all children should be intentionally inoculated by scientifically regulated injections and carefully watched until complete immunity is produced: this, instead of the haphazard and unwatched infections of ordinary childhood. However, whether inoculation is intentional or accidental, this brings us to a vital point of attack in our warfare against tuberculosis, namely, watching the children and young adults, detecting by frequent examination when the mild infection occurs, how it behaves, when it threatens to develop into actual disease, avoiding such diseases as measles and whooping cough which open the way for tuberculosis, and taking measures to keep the health up to par, so that disease does not develop. In this connection, I wish to urge that the periodic examination of children should be an expert and thorough correlation of physical and X-ray examinations and laboratory tests. Childhood tuberculosis takes various forms, and we need to be keenly watchful for its warning symptoms.

Returning to the metaphor of a chain of many links, I will, in closing outline the now famous Framingham experiment in which, in an average town in Massachusetts, an attempt has been made to supply all of the links and to forge them into an effective chain, a complete public health program.

This demonstration is now in its fifth year. The cost has not been excessive, and the experiment has been a pronounced success, a practical lesson of national importance. It was initiated by the Metropolitan Life Insurance Company which offered $100,000 for a three years' community experiment. It was organized by the National Tuberculosis Association and has had the best assistance and coöperation of the community itself.

Some of the chief problems upon which this demonstration attempts to throw light are:

1. Is it possible to discover and to place under adequate medical, nursing and relief supervision all of the cases of tuberculosis, incipient and advanced, active and arrested, in a normal community?

2. Is it possible to ascertain with some degree of definiteness, the responsible social and economic factors in disease causation, particularly as regards tuberculosis?

3. How can social forces best be used to prevent unnecessary sickness and death, particularly from tuberculosis? Practically, what is the best community health machinery for meeting these ends, and what are the essential factors in an adequate preventive, detective and remedial mechanism?

The activities of the Community Health Station have included the voluntary expert examination of almost the whole population of Framingham; a special effort to discover and to place under treatment or observation incipient, advanced or arrested cases of tuberculosis; a sanitary survey, covering infant conditions, schools, factories, food, milk, rural sanitation, vital statistics, etc.; a health census; a patriotic census of the industrial and man power resources of Framingham, eliciting extensive social and economic data; a Pirquet tuberculin survey of children between the ages of one and seven years; a health camp for children; the working out of tuberculosis standards for diagnosis, classification, and treatment of children and adults; domestic science and home economic classes; the development of health educational work, etc.

In addition, there is community organization, financed almost entirely by the community itself and including a group of neighborhood lay committees for education, sickness reporting and similar activities; a community-wide civic association functioning along lines such as recreation, etc.; infant welfare clinics, nursing service, full time medical, nursing and clinic service for the public schools and for the larger industries; community houses for social and health work; a medical club conducting a series of postgraduate instruction clinics and lectures on tuberculosis and allied problems; domestic science classes, under the direction of the home economic instructors at the State Normal School located in Framingham, etc.

The national committee in charge of this demonstration has published a series of monographs describing the work in detail and telling the results. These I recommend for study to every one interested in an effective tuberculosis and public health campaign.

Part of the necessary machinery is, of course, institutional. Hospital facilities have to be provided for the treatment of all forms of tuberculosis. But you can see how limited is the field of institutional treatment when you get a glimpse of the whole broad and comprehensive program.

The Framingham experiment has had the hearty coöperation of Federal and State governmental agencies, town government, private civic associations, charities, churches, clubs, schools, physicians, industrial employers and individual citizens. Here in Canada we have an intelligent and forward-looking people who surely would lend equally good support to as good an organized health campaign. That the tuberculosis problem is complex and far-reaching, we all realize. Some such complex and comprehensive scheme will be needed to cope with it effectually. The doctors and public health workers cannot do it alone. They must teach and lead and be prepared to aid in organization, but, when the chain is complete and all its links strengthened, there will have to be a strong pull and a long pull and a pull all together.

SEVEN YEARS' EXPERIENCE WITH ARTIFICIAL PNEUMOTHORAX[1]

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Induction of artificial pneumothorax as a palliative or curative measure in selected cases of pulmonary tuberculosis, where compression of the whole or part of the lung is required, is the method of choice for patients who fail to respond to the usual hygienic-dietetic or rest-cure treatment. It has grown in favor particularly since 1910; and the striking results obtained in cases that have hitherto been considered hopeless have led to its more extensive application among progressive phthisiotherapists. A full discussion of the indications for compression of the lung in pulmonary tuberculosis may be found in the publications of Riviere, Davies, Garre and Quincke; and the method employed by us will be referred to only briefly.

In the cases reported upon in this paper, as in all of our cases, the patient had been under observation from one to six months before compression of the lung was undertaken. A short time before the operation, generally a week or less, each patient was given a careful physical and fluoroscopic examination and stereoroentgenograms were taken of the chest. If there were no contraindications, the operation was proceeded with. But I should state that, of the first twenty-one patients numbered in this table, none had X-ray examinations, as we had no X-ray apparatus at that time; and further, that several of these attempts were made only because of urgent request on the part of the patient or his family.

The pneumothorax apparatus used by us has been that of Robinson and Floyd; although any two bottles, of appropriate size, graduated in 50 or 100 cc. divisions and connected with rubber tubing to a manometer column, will serve the purpose as well. The needle for the initial injection is the Robinson and Floyd, or the Küss, and for refills a no. 18 gauge Luer needle is invariably used.

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[1] Read at a meeting of the Canadian Medical Association, Halifax, Nova Scotia, July 6, 1921.

Rigid asepsis is observed in all operations. This must be emphasized as invariably necessary to the avoidance of serious complications. Novocain, one-half of one per cent, and adrenalin, 1 to 10,000, is the solution used as a local anaesthetic. It has not been found necessary to give morphine beforehand. Codeine or heroin is given generally one-half hour before the operation. The most convenient area for puncturing the chest is usually in the anterior and posterior axillary folds, in the 5th, 6th or 7th interspace. Filtered air is used, as there is no advantage from employing nitrogen or oxygen gas. The amount of filtered air introduced at the first injection is 200 cc. in some of the cases and 300 cc. in others. This amount is rarely exceeded at the beginning of treatment except in a case of hemoptysis. For the first two or three weeks of treatment, refills of the same quantity are given every second or third day; and then the quantity of gas is increased to 400 cc., occasionally to 500 cc., and injected every four to seven days until the collapse is complete. Subsequent refills are then given at intervals of twelve to twenty-one days as long as the patient remains under observation. I may explain that one of the lessons learned by experience is the giving of small initial injections of 200 cc. and 300 cc. of air rather than the large amounts formerly used; and also that, throughout the treatment, small frequent doses, usually not larger than 400 cc. or 500 cc., are preferable to larger injections at longer intervals. When adhesions are present, the amount of gas injected is determined entirely by the pressures registered by the manometer. Patients who are up and about remain quiet for twenty-four hours following the operation and then come to their meals as usual. The routine of bed patients is not interfered with.

We record our pneumothorax work on individual case sheets and we sum up each case on a case summary sheet.

The present study embraces a group of 65 cases that have been carefully treated and accurately followed for periods of from one to seven years. Of these, 10, or 15.3 per cent, were found to be impossible, and are not considered among the treated. In the "impossible" group operation was attempted, in many, several times; but on account of the pleural membranes being adherent the attempts had to be discontinued. We also considered "impossible" those cases in which less than 100 cc. of gas could be injected into the pleural cavity. Of the remaining 55 patients, 14 are still continuing treatment. Five of these have been treated too short a time for results to be determined, and these are, therefore, not included in this study. Fifty cases are reported upon in the accompanying table.

From our table it will be seen that 13, or 26 per cent, of patients treated were in the moderately advanced or second stage of tuberculosis, and 37, or 74 per cent, were in the far advanced or third stage. Forty-three, or 86 per cent, had tubercle bacilli in the sputum at some time. This treatment was not given to any patient in the incipient or first stage of tuberculosis, as it is generally recognized that the majority of these patients will recover under the usual hygienic-dietetic measures alone.

It will be noted that 14, or 28 per cent, of these patients had unilateral and 36, or 72 per cent, bilateral involvement. In the bilateral cases, the treated lung was usually extensively involved, with cavitation in one or more lobes, while in the untreated lung the disease was, as a rule, inactive, and confined to a small area, not greater than one or two intercostal spaces in extent.

The intention was curative in 24 or 48 per cent; palliative in 13 or 26 per cent; and to stop hemoptysis in 13 or 26 per cent. In certain cases which were considered hopeless from the standpoint of a cure, we nevertheless tried artificial pneumothorax to relieve symptoms such as fever, excessive cough, expectoration, etc.: that is, we tried it as a palliative measure, and frequently got very good immediate results, and even permanent improvement in some cases. For the control of pulmonary bleeding, the results obtained by artificial pneumothorax were in some cases truly dramatic. In other hemoptysis cases, either because of inability to produce sufficient compression, or because of the impossiblity of determining from which lung the bleeding came, the results were disappointing. The side treated was the right in 16, or 32 per cent; and the left in 34, or 68 per cent.

One of the chief obstacles to successful induction of artificial pneumothorax is the presence of intrapleural adhesions. In our table we have taken note of these only when they proved to be a handicap in obtaining a therapeutic compression. These number 26, or 52 per cent, of our cases. In some, the adhesions broke away gradually and safely after gas was introduced. In one case only, which I shall mention when I come to complications, the breaking away of an adhesion adjacent to a cavity caused spontaneous pneumothorax. From this the patient fortunately recovered and is apparently none the worse.

Among the 35 cases abandoned, there were 9 in which adhesions prevented compression of the lung; 14 others in which for one reason or another the patient had to return home and could not come at regular intervals for refills; 10 in which treatment had to be stopped on account of the lighting up of disease in the untreated lung, which was evidently unable to cope with the extra work thrown upon it; and 2 were given up on account of spontaneous pneumothorax in the treated lung. In 3 cases treatment was discontinued because it was no longer necessary. Of the three patients who died during the course of treatment one was hopeless, having profuse and recurrent hemoptyses, for whom pneumothorax treatment was tried as a last resort, one committed suicide, and one developed spontaneous pneumothorax of the untreated side. The remainder are still continuing artificial pneumothorax treatment.

The most frequent complication of this treatment is the development of pleurisy with effusion. The effusion may appear during the production of the collapse or at any time during the maintenance of compression. This occurred in 8, or 16 per cent, of our cases. Other complications in our experience include one case of pleural shock, one of spontaneous pneumothorax of the treated lung, one of apical empyema and one of slight subcutaneous emphysema. None of these has been attended with serious results. This extreme rarity of complications is probably due to exceedingly careful technique, which it is most necessary to observe.

It will be noted that, of those in which the injection of 100 cc. or more of gas was possible, the compression was practically complete in 14, or 28 per cent; partial in 35, or 70 per cent; and a failure in one, or 2 per cent. It must be stated that some of our good results were obtained in cases in which only a partial compression could be induced. On the other hand, in many of our "partial" group the compression was too slight to give any appreciable end results, as will be seen from the following percentages. Our end results were

Excellent	in 4 or 8 per cent
Satisfactory	in 16 or 32 per cent
Fair	in 11 or 22 per cent
None	in 19 or 38 per cent

The end results are those at the conclusion of treatment. Whether these results are durable or not, we attempted to ascertain in those cases in which a year or more has elapsed since the conclusion of treatment, and we find that the present condition of all patients, one to seven years after treatment, is

Well and working	17 or 34 per cent
Living but not working	16 or 32 per cent
Dead	17 or 34 per cent

Taking into account the type of cases that we have treated and the fact that we had 32 per cent of satisfactory end results in addition to a few that we must call excellent; in fact, taking our pneumothorax experience as a whole, we are inclined to agree with other workers that this operation holds out a hope to many tuberculosis patients who, without it, seem unable to recover. We are using it more frequently every year, and we intend to continue its use. We have not as yet been able to make a comparative study of a group of cases treated by induced pneumothorax in addition to the ordinary treatment and a group of similar cases receiving the ordinary treatment without pneumothorax, so as to get an idea of the broad, general value of the latter method. We hope to make such a study at some time in the future.

A drawback to freer use of artificial pneumothorax is the fact that comparatively few patients can afford to remain for many months at or near a sanatorium or health resort, within reach of a physician trained and experienced in its technique. If such a physician were to be found in some of our larger towns, cases having to leave the sanatorium after compression of the lung is well established might be able to continue the treatment at their homes. Many of our cases had to be abandoned because discharged patients found the distance and inconvenience too great for them to come at regular intervals for refills. And we find that if the patient goes even a little too long without a refill, a partial expansion of the compressed lung may permit the formation of adhesions which prevent any further pneumothorax treatment. However, considering the care we find it necessary to give in supervising these cases, the frequent physical and fluoroscopic examinations, etc., our opinion at present is that an institution is the best place at which to receive this treatment.

As to how long compression must be maintained, no general statements can be made. In some cases a few months' complete rest of the lung seems to have started the patient on the road to recovery. In others, especially where cavitation is extensive, compression must be maintained for years, or indefinitely. We have one patient whose

Artificial pneumothorax; summary of cases with regard to results of treatment. Nova Scotia Sanatorium, 1914 to 1921

CASE NUMBER	SEX AND AGE	PATIENT'S CONDITION AT BEGINNING OF TREATMENT							OBJECT OF TREATMENT			HISTORY OF TREATMENT											PRESENT CONDITION OF PATIENT ONE TO SEVEN YEARS AFTER TREATMENT			YEARS AFTER TREATMENT CEASED	REMARKS
		Stage of disease			Involvement		Tubercle bacilli		Palliative			Side treated				Compression			End results								
		Incipient	Moderately advanced	Far advanced	Right lung	Left lung	Tubercle bacilli present at any time	Tuberculous complications	To stop hemoptysis	To relieve other symptoms	Curative	Right	Left	Adhesions encountered	Operative complications	Complete	Partial	None	Excellent	Satisfactory	Fair	None	Working	Living, not working	Dead		
2	M. 37		×		×	×	+		×			×		×			×			×			×			7	Patient returned home
3	F. 30		×		×		0		×			×					×			×			×			7	Patient returned home
5	F. 19		×		×	×	+			×		×		×			×					×			×	3 mos.	Abandoned: extension of disease
6	F. 38			×	×	×	+			×			×		Pleurisy with effusion		×					×			×	1	Abandoned: extension of disease
7	F. 44			×	×	×	+	Tb. pneumonia		×			×				×					×			×	0	Abandoned: extension of disease
8	M. 28			×	×	×	0				×	×		×			×			×			×			7	Abandoned: formation of adhesions
9	M. 24			×		×	+				×		×				×			×					×	0	Suicide
10	F. 22			×	×	×	+			×			×	×			×					×			×	3 mos.	Abandoned: extension of disease
11	M. 21			×	×	×	+				×	×		×		×				×			×				Continuing treatment (6 years)
12	M. 22			×	×	×	0		×				×				×			×			×			6	Continuing treatment (elsewhere)
13	M. 27			×	×	×	+				×		×	×			×				×				×	9 mos.	Abandoned: patient returned home

14	M. 27			×	×	×	+		×				×	×			×					×			×	1 mo.	Abandoned: extension of disease
15	M. 18			×	×	×	+		×				×			×			×					×		5	Discontinued: no longer needed
16	M. 30			×	×	×	0		×			×					×			×					×	2	Patient returned home
17	M. 28			×	×	×	+				×		×		Pleurisy with effusion	×				×			×			4	Patient returned home
19	F. 44			×	×	×	+				×		×			×					×		×			5	Patient returned home
20	M. 21			×	×	×	+			×		×		×			×					×			×	6 mos.	Abandoned: extension of disease
21	F. 25			×	×	×	+	Tb. laryngitis		×		×		×			×					×			×	1 mo.	Abandoned: extension of disease
22	M. 26			×	×		+	Ischio-rectal abscess		×		×					×			×				×		3	Patient returned home
23	M. 29		×		×	×	+				×		×	×			×				×		×				Continuing treatment (3 years)
24	M. 23		×			×	+				×		×	×			×			×			×				Continuing treatment (3 years)
25	F. 24		×		×		+				×	×		×			×				×		×			2	Abandoned: formation of adhesions
26	F. 19		×			×	+				×		×				×					×			×	2	Abandoned: adhesions
27	F. 31			×	×	×	+				×		×				×					×			×	2	Abandoned: extension of disease
28	F. 22		×			×	0		×				×				×			×			×			3	Abandoned: patient at home
29	M. 38		×		×	×	+				×		×	×			×			×			×			2	Abandoned: adhesions
30	M. 23			×	×	×	+				×		×	×			×					×			×	0	Fatal spontaneous pneumothorax of untreated side
31	M. 40		×		×	×	+				×		×			×			×				×			2	Discontinued: no further need
32	M. 40			×	×	×	+			×			×	×	Pleural shock		×					×			×	2	Abandoned: formation of adhesions
33	M. 21			×	×		+				×	×		×	Apical empyema		×				×			×		1	Abandoned: formation of adhesions
34	M. 19			×	×	×	0				×		×				×				×			×		2	Patient returned home
35	M. 25			×	×	×	+				×		×		Pleurisy with effusion		×					×		×		1	Abandoned: adhesions

Artificial pneumothorax; summary of cases—Concluded

CASE NUMBER	SEX AND AGE	PATIENT'S CONDITION AT BEGINNING OF TREATMENT							OBJECT OF TREATMENT			HISTORY OF TREATMENT											PRESENT CONDITION OF PATIENT ONE TO SEVEN YEARS AFTER TREATMENT			YEARS AFTER TREATMENT CEASED	REMARKS
		Stage of disease			Involvement		Tubercle bacilli		Palliative			Side treated				Compression			End results								
		Incipient	Moderately advanced	Far advanced	Right lung	Left lung	Tubercle bacilli present at any time	Tuberculous complications	To stop hemoptysis	To relieve other symptoms	Curative	Right	Left	Adhesions encountered	Operative complications	Complete	Partial	None	Excellent	Satisfactory	Fair	None	Working	Living, not working	Dead		
36	M. 22			×	×	×	+		×				×			×						×			×	1	Abandoned: extension of disease
37	M. 32			×	×	×	+				×	×		×	Pleurisy with effusion	×					×		×			1	Patient returned home
38	F. 36			×	×	×	+				×	×		×		×				×			×				Continuing treatment (2 years)
40	M. 18		×			×	0		×				×			×			×				×			3 mos.	Discontinued: no further need
41	M. 19			×		×	+	Ischio-rectal abscess		×			×		Pleurisy with effusion		×				×			×		6 mos.	Patient returned home
43	M. 25			×		×	+				×		×	×	Pleurisy with effusion	×			×					×			Continuing treatment at home (2 years)
44	M. 25			×	×	×	+		×			×					×					×			×	0	Profuse hemoptyses; fatal
45	M. 27			×	×	×	+				×		×	×	Pleurisy with effusion		×				×			×		1	Patient returned home
46	M. 25		×			×	+				×		×	×				×				×			×	5 mos.	Abandoned: adhesions
47	M. 22		×		×	×	+				×		×			×					×			×		1 mo.	Patient returned home

48	M. 23			×	×	×	+			×		×			Tb. pyopneumothorax: spontaneous pneumothorax of treated side	×						×		×		1	Abandoned: spontaneous pneumothorax of treated side
49	M. 24			×		×	+				×		×		Pleurisy with effusion	×				×				×			Continuing treatment (1½ years)
50	M. 27			×	×	×	+				×		×	×			×					×		×		1	Abandoned: adhesions
52	M. 34			×	×	×	+	Tb. laryngitis	×			×		×			×					×	×			1	Patient returned home
53	M. 21			×	×	×	+		×				×	×			×			×				×			Continuing treatment elsewhere
56	F. 22			×	×	×	+	Tb. laryngitis		×			×	×			×			×				×			Continuing treatment (8 months)
58	M. 24			×	×	×	+		×				×			×					×			×		6 mos.	Abandoned: extension of disease
61	F. 25			×		×	+			×			×	×	Spontaneous penumothorax (complete) of treated side		×					×		×			Abandoned: spontaneous pneumothorax of treated side
Totals			13	37	40	46	43		13	12	25	16	34	26		14	35	1	4	16	11	19	17	16	17		

Unilateral 14, bilateral 36.

right lung has been completely compressed for six years and it cannot yet be allowed to expand.

CONCLUSIONS

1. Induction of artificial pneumothorax should not be attempted in bilateral tuberculosis when both lungs show evidence of progressive disease.

2. In no far advanced case of pulmonary tuberculosis where the progress made under ordinary treatment is unsatisfactory should the patient be refused treatment by artificial pneumothorax, provided there is one lung in which there is little or no disease, and provided also that there are no serious complications.

3. As a means for the stopping of hemoptysis, provided it is known from which side the bleeding comes, artificial pneumothorax has a distinct value.

4. Merely as a palliative measure, artificial pneumothorax has its value in the relief of symptoms.

5. Our experience has proved that even a partial collapse of the lung may be followed in some cases by appreciably good results.

6. In cases where artificial pneumothorax is indicated, it should not be postponed until the patient has drifted into such a condition that intrapleural adhesions prevent therapeutic compression of the lung.

7. In most cases of extensive disease, in order to obtain durable results, compression should be maintained for a year or longer.

My thanks are due to Drs. R. J. Collins, T. M. Sieniewicz and C. M. Bayne, and to Mr. H. Hamon, roentgenologist, for their valuable part in our artificial pneumothorax work.

TUBERCULOUS PYOPNEUMOTHORAX TREATED WITH METHYLENE BLUE

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About a year and a half ago we had occasion to inject a solution of methylene blue into the pleural cavity of a patient who was suffering from a localized pyopneumothorax. This was done with a view of determining the presence of a bronchial fistula. The diagnosis was confirmed when the patient expectorated the methylene blue immediately after its introduction into the pleural cavity.

Incidentally, we were surprised to notice a marked fall in the patient's temperature after the injection of the drug. The patient's general condition has also definitely, though only temporarily, improved. It then occurred to us that the methylene blue might have exerted a beneficial influence on the pyopneumothorax and that this agent might prove to be of value in the treatment of this condition. But, inasmuch as the patient in whom the methylene blue was first tried had only a localized pyopneumothorax which was draining well through the fistula and he was not doing well on account of a progressive, active, bilateral pulmonary lesion, it was impractical to continue treating him with methylene blue. Soon, however, we had an opportunity to use this treatment in two patients who developed tuberculous empyema during the course of therapeutic pneumothorax. The pus from the pleural cavity was aspirated and replaced by sterile air, and at the end of the operation 2 to 3 cc. of a saturated alcoholic solution of methylene blue was injected into the pleural cavity through the aspirating needle. These patients improved so markedly that we feel justified in recommending this drug in the treatment of pyopneumothorax.

REPORT OF CASES

Case 1. A. J., a female school teacher, twenty-two years of age, was admitted to Bedford Sanatorium in November, 1919. She stated that her present illness began with an attack of influenza eleven months before admission. Since then she had considerable cough and expectoration and frequent afternoon fever reaching to 101° F. She also lost considerable weight and strength and had frequent pains in the right side of her chest.

Examination: Physical examination on admission disclosed considerable dulness and feeble breathing from the lower angle of the scapula to the base on the right side. Numerous moist râles were audible at the lower half of the chest anteriorly and posteriorly. Examination several days later disclosed evidence of a large cavity at the right base posteriorly. Roentgenological examination confirmed the physical findings. Her sputum was positive for tubercle bacilli; her urine was negative.

Course and treatment: While at the sanatorium, the patient ran an active course. She had considerable fever, distressing cough and expectoration and frequent night sweats. She also lost much weight and strength. A right pneumothorax was induced in January, 1920, and a fair collapse was obtained. But, due to the fact that the large cavity at the base could not be successfully collapsed, the patient improved but slightly during the first few weeks of treatment.

On February 8, 1920, the patient developed severe pain in the right chest, chills, fever up to 105° F., and extreme prostration. Evidence of pleural effusion was elicited several days later. Assuming that the patient was developing an ordinary serous effusion, she was left alone, in the hope that the acute symptoms would soon subside. But the fever and the other distressing symptoms continued for weeks and the patient's condition was very grave.

On April 10, 1920, a pleural puncture revealed a purulent effusion. Thirteen hundred cubic centimetres of the pus were then removed and replaced by sterile air. Another aspiration was done on April 26, when 200 cc. of pus was withdrawn and replaced by air. At that time 2 cc. of a saturated alcoholic solution of methylene blue was introduced into the pleural cavity through the aspirating needle, and similar treatment has been continued at definite intervals for about one year, when the pus no longer accumulated and a tendency to organization was noted.

Soon after the injection of the methylene blue, the patient's condition took a decided turn for the better; the fever gradually subsided and the patient began to gain weight and strength. At present she is practically free from any symptoms, has gained about 20 pounds in weight, her sputum has been negative for tubercle bacilli for six months, and she is doing several hours work every day.

Bacteriological examination of the pus after the first aspiration revealed numerous tubercle bacilli on direct smear. Later the number of tubercle bacilli in the aspirated pus markedly decreased, and those that were found were reported by the bacteriologist to be "slender, beaded, and apparently degenerated."

A guinea pig was inoculated with the pus aspirated on March 17, 1921. The animal was killed and autopsied on May 18, 1921, and no evidence of tuberculosis was found.

Case 2. O. C., a male physician, thirty-nine years of age, was admitted to the Bedford Sanatorium on July 23, 1919. He gave a typical history of moderately active pulmonary tuberculosis of three years' duration. He had been treated in several institutions without much amelioration of his symptoms. A right pneumothorax was induced at the Loomis Sanatorium in March, 1918.

Examination: Physical examination on admission to our sanatorium revealed an extensive pneumothorax on the right side. The left lung was apparently clear. There was no evidence of pleural effusion. Roentgenological examination confirmed the physical findings. His sputum was positive for tubercle bacilli; his urine was negative and his temperature and pulse rate were normal.

Course and treatment: During the first few months of the patient's stay at the sanatorium, he was doing fairly well. His temperature and pulse rate remained normal and he gained some weight, but he was still complaining of considerable cough and expectoration and moderate dyspnea. The pneumothorax treatments were continued at the usual intervals.

On January 22, 1920, the patient was taken acutely ill with fever up to 104° F., accelerated pulse and respiratory rate, and extreme prostration. Evidence of pleural effusion was soon elicited. On February 24, 1920, an exploratory puncture revealed clear fluid. The patient was treated expectantly, as we hoped the acute symptoms would subside. But, contrary to our expectations, the severe and distressing symptoms continued for weeks and the patient's condition became very grave. On April 23, another puncture revealed purulent fluid. Eighteen hundred cubic centimetres of pus were then aspirated and replaced by 900 cc. of sterile air. The patient felt somewhat relieved, but his general condition remained quite serious.

On May 3, 1920, 1100 cc. of pus were aspirated and replaced by 900 cc. of air. At this time 3 cc. of methylene blue was injected through the aspirating needle. The same treatment has been continued to the present time, the intervals between treatments being increased as the accumulation of the fluid decreases. There was a most remarkable change for the better in the patient's condition within one day after the injection of the methylene blue and the improvement has constantly continued. His temperature gradually came down to normal and he has gained 34 pounds in weight. His sputum has been negative for tubercle bacilli since August, 1920, and in April, 1921, the patient resumed the practice of medicine.

Bacteriological examination of the pus after the first few aspirations showed numerous tubercle bacilli on direct smear, the microscopic appearance of the smear being that of a pure culture of tubercle bacilli. The number of bacilli has gradually decreased and recently only a few can be found in the smear.

A guinea pig was inoculated with the pus on April 14, 1921, and the animal was etherized on May 21, 1921. The autopsy revealed typical tuberculosis.

COMMENT

In view of the fact that the prognosis in tuberculous pyopneumothorax is decidedly grave, the favorable outcome of these two cases could hardly be attributed to chance. Furthermore, the marked improvement in both these patients followed the injection of methylene blue so promptly, that it is more than likely that the latter was to a great extent responsible for the results obtained.

We used the methylene blue rather empirically and without knowledge that it had at some time been used in the treatment of such cases. A search of the literature, however, disclosed the fact that methylene blue, as well as other dye substances, have, at one time or another, been considered of definite value in similar cases.

Lewis (1) in 1899 injected methylene blue into the pleural cavity of patients suffering from serous effusions, for the purpose of promoting absorption from the pleural cavity and stimulating the formation of pleuritic adhesions, thus preventing further accumulation. He injected as much as 12 grains of methylene blue without any untoward results.

In 1915, Nobecourt (2) and his co-workers treated cases of empyema following bronchopneumonia, with injections into the pleural cavity of 10 cc. of a 5 per cent watery solution of methylene blue, following the aspiration of the pus, and they report excellent results.

Other aniline dyes have also been used for similar purposes. Churchman (3) used a solution of gentian violet in the treatment of infected joints and he reported good results. Following the suggestion of Churchman, Waters (4) used a dilute solution of gentian violet for irrigation of the pleural cavity in cases of pyogenic infection of the pleura complicating artificial pneumothorax.

The work of Lewis and DeWitt (5) offers a rational basis for this mode of therapy. These observers have shown that methylene blue inhibits the growth of tubercle bacilli in solutions of one to one thousand. DeWitt (6) has also shown that moderate concentrations of methylene blue will kill tubercle bacilli *in vivo* as well as *in vitro*. In this connection it is pertinent to recall that the pleural pus in one of our cases failed to infect a guinea pig, in spite of the fact that acid-fast bacilli were found on direct smear. Besides its antiseptic value, methylene blue stimulates organization and fibrous tissue formation, thus aiding nature in combating the tubercle bacillus. That methylene blue is capable of stimulating fibrous tissue formation with a minimum amount of irritation, has been brought out by Lewis (1), after he tested many substances that were suggested for that purpose.

Methylene blue, unlike most antiseptics has a very low toxicity and considerable amounts can be injected without producing any untoward results. Its use is not attended by symptoms of pleural irritation. It is slowly absorbed from the pleural cavity, as evidenced by the fact that the urine retained a blue tinge for at least ten days after each injection.

We used a saturated alcoholic solution, because it is easily prepared and requires no sterilization In view of the fact that only a very small amount of pus was left after each aspiration, we thought 3 cc. of a saturated solution would be sufficient to produce the desired effect. We are certain, however, that larger amounts can be injected without any ill effects.

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THE SAFE REMOVAL OF TONSILS BY THE DESICCATION METHOD WITH THE HIGH FREQUENCY CURRENT IN POOR SURGICAL RISKS, WITH ESPECIAL REFERENCE TO TUBERCULOSIS[1]

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Diseased tonsils quite frequently play an important part in impeding the tuberculous patient's progress toward recovery. The employment of the usual surgical methods for their removal, which is comparatively safe for the otherwise healthy patient, entails rather serious risks for the tuberculous. The mental strain, the loss of blood during the operation, and the marked soreness, preventing as it does the taking of food for several days, are necessary evils of the surgical operation which often materially lower the patient's vitality. When we consider the fact, too, that rather serious complications may occur, such as pulmonary abscess, secondary hemorrhage, pneumonia, embolism and infection, the danger of the surgical operation for the tuberculous patient is all the more real.

Unfortunately the tonsils of the tuberculous are equally, if not more, subject to ordinary diseases and, in addition, are much more frequently than others the seat of tuberculous lesions either active or latent. Weller (1) states that the histological examination of material from 8,697 consecutive tonsillectomies at the University of Michigan showed active tuberculosis in 2.35 per cent. Ballenger (2) states that various writers report from 4 to 10 per cent of tonsils removed for all causes as showing local tuberculous lesions. Wood (3) reports the tonsils involved in 88 per cent of 43 of his own cases of tuberculosis coming to autopsy and in 69 per cent of 167 tuberculous patients reported by 7 other investigators.

The presence of tubercles in tonsils constitutes an additional element of danger for their surgical removal because of the possibility of disseminating the infection. The necessary trauma and the gaping blood vessels of the peritonsillar tissue make such an eventuality not improbable. In cases of active tuberculous ulceration the danger is so real as to constitute a contraindication to the ordinary tonsillectomy. Yet, if such a tonsil is not removed, the patient soon becomes the victim of tuberculosis of the pharynx and the neighboring structures, which is the most to be dreaded of all complications.

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It was such a dilemma as his which occasioned our learning of the use of the high frequency current for the removal of tonsils. A recent graduate of one of the best medical colleges in Philadelphia, who had been a former patient of ours, had an exacerbation of his trouble while taking his interneship in one of the large hospitals in the same city. He returned to us with active symptoms, tubercle bacilli in his sputum and an ulcerated left tonsil, only the shell of which was left. We felt that surgery was contraindicated, but thought there was possibility of relief through cauterization, and sent him back to consult his professor of diseases of the nose and throat. After confirming the diagnosis of tuberculosis of the tonsil by removing a small section for microscopical examination, the latter sent him to Dr. Wm. L. Clark, of Philadelphia, who removed the tonsil by the desiccation method with the high frequency current. After two weeks he returned with no sign of any tuberculous process in his throat, his active symptoms disappeared, and at the end of two months he went on our staff and continued doing regular work with no return of symptoms.

We secured a high frequency machine and have used the method over a period of four years in 32 cases. In 1918 Clark (4) reported his results in over 50 cases, and our experience coincides with that as stated by him: "The desiccation method may be depended upon to fulfill every requirement, namely, sterilization, complete or partial removal of tonsils without surgical shock, hemorrhage, or great immediate or after discomfort to the patient, and with no resulting contracted cicatrix or danger of impairment of phonation." This is the only method which is at all safe for the removal of ulcerated tuberculous tonsils, and it is not only safe but, where the process is limited to the tonsils themselves, it can practically always effect a cure.

Oftentimes it is not necessary to remove a whole tonsil, for frequently the source of the trouble comes from the retained infected material in only a few of the crypts. This is most commonly true in the crypt opening into the supratonsillar fossa and at the base of the posterior pillar, where the tonsil is capped over by folds of mucous membrane which may hug so tightly as to close the mouths of the crypts. By the desiccation method it is a comparatively simple matter to destroy enough of the tonsil to establish free drainage of these crypts; and in case the morbid local and general processes do not subside following this, the remainder of the tonsil may be removed at a later date. This has the double advantage of conserving all healthy tonsillar tissue for any useful purpose it may serve and of causing the least possible inconvenience to the patient from the operation.

The only special equipment needed is a standard high frequency machine, a fulguration handle with suitable electrodes and a foot switch, all of which can be had with an outlay of about two hundred dollars, or perhaps less. It is the monopolar Oudin current which is employed. We use the little aluminum wire electrodes insulated with rubber tubing. The aluminum permits bending of the tip of the electrode to any desired angle, so that any part of the tonsil may be reached. The foot switch is essential in order that the current may be turned off instantly when necessary.

The destruction of the tissues is accomplished by sparks from the electrode which cause dehydration or desiccation. The tip of the electrode should be held in contact with the tonsil, since any air space will prevent penetration. The current should not be strong enough to cauterize. The destruction may be carried to any depth desired, and either one or both tonsils may be removed at one sitting. The best results, however, can be obtained by destroying the tissues to only a small depth at one sitting and allowing sufficient time between treatments for the destroyed tissues to come away. It usually requires two or three sittings, at intervals of three to seven days, to completely remove a tonsil. By following this procedure tuberculous patients have so little soreness following the operation that they do not have to miss a single meal, they are not confined to bed and they have but little if any fever.

We follow in the main the technique as described by Clark (4). The operation is carried out with the patient sitting in a comfortable chair with a head rest. The only anesthetic ordinarily needed is a topical application of an 8 to 10 per cent cocaine or novocaine solution. Rarely, in sensitive throats, 0.5 to 2 per cent novocaine or procaine, injected only into the tonsil, will be necessary in addition to the above to make the procedure painless. The reflexes are destroyed by an application of the solution to the pharynx and the neighboring structures. Several applications are made to the tonsils and a sufficient time is allowed for the drug to take effect, which is usually ten to twenty minutes. The tonsils are not very sensitive to pain; but the pillars, tongue and uvula are quite sensitive, and great caution needs to be exercised to avoid touching them in applying the current. This was the source of error in the few cases which we have had to suffer any degree of pain or to have more than a slight amount of secondary inflammation following the operation. The tongue is kept out of the way by using a rather large tongue depressor, which is held, after being placed in the desired position, by the patient himself. This is not only a convenience to the operator but it has also a helpful psychological effect on the patient. At the first sitting a pillar retractor is usually not necessary, but after the more prominent portion of the tonsil is removed, it is necessary to retract the anterior pillar, in order that the part of the tonsil lying behind it may be brought into view for removal. For this purpose an instrument should be used, the edges of which are smooth and rounded, so that there will be a minimum amount of discomfort on traction.

Our experience has been limited to adults. Naturally the method is not applicable without a general anesthetic in young children. But it is my opinion that it could be used as in adults in a good many children of intelligence of seven or eight years or older. We have had occasion also to use it only in cases of tuberculosis. There is no reason, however, why it should not be used in any condition such as cardiac and renal diseases, the anemias and hemophilia, in which surgery is contraindicated. The only disadvantages of the method are that it cannot be used in young children and that it requires more time and patience.

The results recently reported by Witherbee (5) through the use of the X-ray in causing atrophy and sterilization of diseased tonsils, are so encouraging that the time may come when a tonsillectomy is rarely necessary. It will never be safe, however, to depend upon the X-ray alone in cases of active tuberculous ulceration of the tonsils. The desiccation method should be used for the removal of such tonsils. But even here the best results can probably be obtained through the combination of the two methods.

The desiccation method can be used best, of course, by a throat specialist, but it can be used safely and with good results by any physician who is careful and who knows the anatomy of the tonsil region. A knowledge of electricity is not necessary. The equipment for its use should be a part of the armamentarium of every sanatorium.

SUMMARY AND CONCLUSIONS

1. The surgical removal of tonsils entails rather serious risks for the tuberculous patient.

2. In cases of active tuberculous ulceration of the tonsil the additional risk of disseminating the infection is so great that surgery is contraindicated.

3. Tonsils, whether the seat of tuberculous lesions or not, can be removed without immediate or after bad results with the high frequency current.

4. The procedure is simple and the equipment is not expensive.

5. The main disadvantage of the method is that it requires more time, since the best results are obtained by light applications of the current at several different sittings.

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UTERINE TUBERCULOSIS ASSOCIATED WITH UTERINE NEOPLASMATA

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The concurrent existence of tuberculosis of the uterus and uterine neoplasmata is seldom considered by the average physician. While it is an uncommon association of diseases, there have been a few cases reported in the literature, and doubtless other cases have occurred which have not been recorded. A search of the literature as recorded in the *Index Catalogue of the Surgeon-General's Library* resulted in the discovery of but seven cases, grouped as follows: two cases of papillary adenomata with uterine tuberculosis, two cases of adenomyomata with tuberculosis of the uterus, two cases of mucous polypi and one case of uterine myoma associated with uterine tuberculosis. To this collection may be added a single case studied by the author, of tuberculosis of the uterine mucosa with a mucous polypus.

Heinrich (1) reports a case of uterine tuberculosis with uterine myomata. It occurred in a patient, fifty-four years of age, a nullipara. There was no antecedent history of tuberculosis in the family. The menopause had occurred at the age of fifty-three. During the four and one-half months previous to her coming under observation she had suffered from almost daily uterine bleeding. She also complained of increasing weakness, severe vertigo, a cough with expectoration of blood-tinged sputum, and fainting spells. On examination, she presented multiple subserous and interstitial fibroids, from which a clinical diagnosis of degenerated uterine myomata was made. Examination of the excised uterus revealed many myomata, subserous and interstitial. The endometrium was much thickened and infiltrated with small miliary tubercles.

There are two instances of polypi in a uterus which was also the seat of tuberculous disease. The first case is that of Zahn (2). This uterus presented a tuberculous ulcer of the endometrium, extending into the myometrium. A mucous polyp was so situated that secondary invasion of the polypus from the tuberculous ulcer occurred. The other case was reported by Michaelis (3). This patient was thirty-three years old, complained of menstrual irregularities, fever and anemia since her last pregnancy. A clinical diagnosis was made of chronic endometritis and curettage was performed. A mucous polypus was discovered. Microscopic examination of the curettings revealed the presence of tuberculosis and the polypus was likewise tuberculous. This was a secondary case, since the left lung presented evidences of tuberculous involvement. Tubercle bacilli were demonstrated both in the curettings and in the polypus.

Two cases of papillary adenoma coexistent with uterine tuberculosis have been reported. Gigloi's (4) patient complained of pelvic pain with menstrual disturbances. On physical examination, the thoracic and abdominal organs appeared normal, the uterus being slightly prolapsed. Vaginal examination showed the cervix transformed into an irregular, fungoid, very friable mass, which apparently arose from the external orifice of the uterus. This mass was somewhat painful on palpation. The uterus was slightly enlarged but was movable. Posteriorly, the uterus gave the impression of being the seat of an elastic tumor. The uterus was removed and histological examination furnished the diagnosis of "chronic tuberculous endometritis with papillary adenoma."

Madelener's case (5) is peculiar in that it illustrates the infection of a polypus indirectly from a tuberculous ovary. The polypus was adenomatous in nature and so situated that it lay in contact with an entirely local caseous focus in the myometrium and endometrium. The focus in the uterine wall was solitary, and evidently owed its origin to the tuberculous ovary, which was adherent to the peritoneal surface of the uterus at a point overlying and closely corresponding to the point of development of the myometrial focus.

Two instances of uterine tuberculosis associated with adenomyomata are found. Archambault's (6) patient was an unmarried girl of twenty who suffered from pulmonary tuberculosis and a growth in the uterus. At operation, the peritoneum and ovaries were normal, while the tubes were tuberculous. The uterus presented an adenomyoma, and in this adenomyoma tuberculosis had secondarily developed. Microscopic examination revealed tubercle bacilli within the neoplasm. Lindquist's (7) case was in a woman of fifty, who was suffering from Basedow's disease. She presented a palpable neoplasm in the uterus. At operation this was found to be an adenomyoma which was the site of tuberculous invasion. Tubercle bacilli were demonstrated within the tissues of the adenomyoma.

The case which occasioned the writing of this paper, occurred in a married woman, aged forty-three years, American, 3-para. The family history was unimportant, there being no history of tuberculosis in the antecedents. The menstrual cycle began at the age of fourteen, and developed into a regular twenty-six day periodicity. There have been three pregnancies, the last occurring thirteen years previous to her seeking advice. No miscarriages. Has had several attacks of influenza, one attack of pneumonia, which yielded to a rather protracted convalescence. The present complaint is that of an excessive loss of blood at the menstrual epochs, which has shown a tendency to increase with succeeding periods. This is accompanied by severe pain in the lumbar region, recently necessitating the patient being confined to her bed during the epochs. These periods last about ten days, during the last two or three days of which the flow gradually decreases. There also is evident a feeling of weight in the pelvis, which is accentuated at the periods. The patient complains of a moderate degree of constipation. On physical examination, the patient appears moderately well nourished, weight 130, with no apparent recent loss of weight. The chest and upper extremities appear normal. The abdomen is negative. The pelvis presents a somewhat enlarged uterus, with a slightly softened feel. The uterus was moderately anteflexed. The perineum was relaxed and the vulva gaping. There was a noticeable loss of tone in the perineum. A clinical diagnosis was made of anteflexion of the uterus, probably due to the relaxation of the perineum. An operation for repair of the perineum was undertaken, previous to which a routine curettage was performed. Microscopic examination of the curettings revealed a mucous polypus, 3 by 1.5 by 1 cm. Sections of the curettings revealed a number of tuberculous ulcers, together with a few miliary tubercles. Sections from the polypus also showed the characteristic picture of tubercle. Sections stained for tubercle bacilli revealed a small number of acid-fast rods. The convalescence was uneventful, the patient being discharged in a satisfactory condition. She returned after several weeks, complaining of a loss of weight and a feeling of fatigue, with a distressing cough. Physical examination at this time revealed a suspicious area in the right apex, which was demonstrated in roentgenograms. The sputum however was negative for tubercle bacilli on repeated examinations.

The symptoms of uterine tuberculosis coexistent with neoplasms do not clearly indicate the presence of the two separate entities. The patient usually complains of menstrual irregularity, usually in the form of intermenstrual bleeding of variable seriousness. Closely associated is the complaint of pain, characterized frequently as a dull, aching pain in the pelvic region, at times radiating down the thigh, at times downward toward the buttock, and occasionally upward toward the dorsal vertebrae. Occasionally there is a complaint of rise in temperature in the afternoon. Increased nervousness and irritability are at times noted. In case of the neoplasm being a rather large fibroid tumor, there may be a complaint of sensations of weight and dragging in the pelvis. In the average case, the patient furnishes very little information which would lead to a suspicion of tuberculosis, although the history may be clearly indicative of the presence of a uterine neoplasm or chronic endometritis.

On examination, there is often found a peculiar anemic condition, which is in part explained by the loss of blood through the menstrual disturbance, but in part is to be attributed to the tuberculous lesion. Palpation may occasionally reveal the presence of the larger neoplasms, but reveals no hint of tuberculosis. The vaginal examination reveals evidences of menorrhagia, accompanied by a varying amount of discharge simulating leucorrhoea. The bimanual examination may reveal the presence of the neoplasm, or may give indication of a retroversion of the uterus due to the new growth. The physical examination, in short, reveals no findings which suggest the presence of tuberculosis.

The pathology varies considerably according to the type of neoplasm present and according to the location of the tuberculous process. The tuberculous lesion may be located in the uterine mucosa of a uterus which contains myofibromata, either submucous, subserous or interstitial. In the instances of tuberculous invasion of a uterus containing polypi, the lesions sometimes localize in the uterine mucosa, at other times develop within the tissues of the polypus. In the reported cases of adenomyoma, the tuberculous process had in each instance localized in the neoplastic tissues, but probably this localization would not hold constant in a larger series of cases.

The diagnosis of this association of diseases is by no means easy. The existence of the neoplasm presents only the usual difficulties, but there is usually little suggestion of the tuberculous lesion. In general, the diagnosis will be made only by those who undertake routine bacteriological examinations of all vaginal discharges. Smears should be made from the vaginal discharge and stained for the demonstration of acid-fast bacilli. If bacilli can be thus demonstrated, animal inoculation should be practised to exclude the presence of nonpathogenic acid-fast organisms. In cases suggesting endometritis, where a curettage is performed, a portion of the curettage fragments should be ground up in a tissue crusher and the juice injected into a laboratory animal, while another portion is embedded in paraffin and examined histologically, staining for acid-fast bacilli if the histological picture is suggestive. If these simple bacteriological manoeuvres were routinely practised in all cases of chronic endometritis, undoubtedly uterine tuberculosis would be detected more frequently.

The differential diagnosis of this condition lies between neoplasmata of the uterus, chronic endometritis, and uterine syphilis. The diagnosis is made by a process of elimination through a combination of microscopic study of the curettings, animal inoculation, and the Wassermann test.

Of the complications, the most serious is pulmonary or general miliary tuberculosis, in which case the uterine lesion is to be considered as a part of the general process. Tuberculous involvement of the Fallopian tubes may occur, although seldom reported. No cases of pregnancy in a uterus which was the site of tuberculosis and a neoplasm have come to my attention.

The prognosis is unfavorable, except in the rare case where the tuberculous lesion is primary in the uterus, and the uterus and its neoplasm can be removed surgically. In cases where there is peritoneal tuberculosis or a coexistent pulmonary or general miliary tuberculosis, the outlook is nearly hopeless.

The treatment should be surgical in those cases where the local disease is primary in nature, and in all cases where the evident lesions in the lungs have been quiescent for some time. The patient should be put in as good a physical condition as possible, and the use of spinal anaesthesia will minimize the danger of activating the pulmonary lesions. In cases where there is active general miliary or pulmonary tuberculosis, the use of a supporting and nourishing diet, absolute rest in bed with fresh air, sunshine and suitable tonics, constitute the only treatment. Heliotherapy might be tried, but its advantages are not well established. The use of roentgen rays and radium have thus far not been particularly inspiring in the treatment of this disease, nor has tuberculin offered any hopeful results.

CONCLUSIONS

1. More attention should be accorded the possibility of tuberculosis of the uterus complicating uterine neoplasms. The cases reported in the literature are few in number; hence similar cases should be reported.

2. The diagnosis is not simple. Increasing weakness, intermenstrual

hemorrhages, slight anemia, and radiating pains whose point of origin is apparently in the pelvis, and the presence of an evident neoplasm should call for careful laboratory investigation.

3. The prognosis is good only in the cases where the uterus is the seat of the primary tuberculous lesion. It is also somewhat favorable in cases where the general systemic or pulmonary process is quiescent or healed. It is unfavorable where the pulmonary or general process is active.

4. The treatment is surgical wherever possible. Active pulmonary or general miliary tuberculosis is a contraindication to surgical treatment. Medical, dietetic and hygienic treatment should be used in nonsurgical cases and in the postoperative cases. Roentgen ray and radium therapy are disappointing.

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THEORETICAL CONSIDERATIONS ON THE APPLICATION OF ULTRAVIOLET RADIATION IN TUBERCULOUS LARYNGITIS[1]

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It is not with the intention of making any special claims for this mode of therapy that this paper is offered. A citation of 35 cases that I have been able thus far to treat would probably impress you favorably just as the results did me. However, we realize only too well the lack of criteria for determining which patients would and which would not heal spontaneously after a sufficient period of time had elapsed. Therefore, adequate proof must necessarily be lacking. What should interest us much more is a consideration of the basic principles, to decide whether or not we may rationally expect that ultraviolet irradiation of an accessible lesion, such as the larynx, can promote healing. This necessarily involves a study of any direct effect of ultraviolet rays upon the body tissues.

Varying claims for reflected light radiations have been made. The majority of workers, until recently, have employed reflected sunlight. Kunwald, Blumenfeld, Sorgo, Jessen, Jansen, Malgat and Vevey abroad, and Mills and Forster and others in America, have all been rather well impressed. Brüning and Albrecht were disappointed in their work with solar rays, while with X-ray radiations they were able to demonstrate some fibrosis. With ultraviolet exposures, Heusner, Ladeback and Pachner have employed reflecting mirror devices and considered their results favorable. X-ray radiations of the larynx have also their exponents (Fleck, Ramdohr, Kümmell and others); some confining them to infiltrative processes, others to ulcerative lesions.

Because an accurate understanding of the rays employed is necessary, both when working with reflected sunlight and with reflected and direct ultraviolet radiations, it becomes essential for us to consider, at least briefly, the light sources and their qualities. Sunlight, as it reaches us both in high altitudes and the lowlands, contains the longer ultraviolet rays, as well as the visible heat, light and actinic rays and the invisible infrared rays; the shorter ultraviolet rays are lacking. In altitudes, the ultraviolet intensity is greater, both in winter and summer, than in lowlands.

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[1] Read before the Clinical Section at the Seventeenth Annual Meeting of the National Tuberculosis Association, New York City, June 15, 1921.

Reflectors made of special metals can eliminate the heat rays, and the ultraviolet reflection may yet prove considerable. Nickel, aluminum, silver, platinum, silicon and magnalium may all be employed. Of these metals, magnalium, an alloy of magnesium and aluminum, is the best reflector of the chemical rays and completely eliminates the heat wave lengths; an objection to it is the ease with which it corrodes. Silicon is difficult to obtain in glazed form. Both of these have the best reflecting properties (85 per cent of the ultraviolet wave-lengths are reflected). The other metals mentioned reflect 35 per cent to 45 per cent. Mirrors of glass are less effective than those of quartz, because of the marked absorption of the ultraviolet rays by the former. Quartz furthermore is less breakable, does not oxidize, and can be easily sterilized by boiling because of its resistance to very high temperatures.

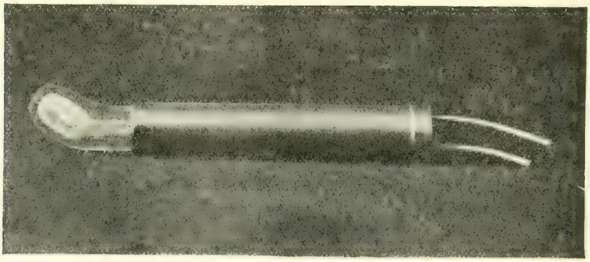

FIG. 1. LARYNGEAL MERCURY QUARTZ LIGHT (WATER-COOLED)

The mercury quartz lights contain an abundance of the short ultraviolet rays, not present in sunlight, as well as the additional longer ultraviolet, blue and violet wave-lengths (all chemically active). Seventy per cent of the radiation emitted by the mercury vapor arc consists of ultraviolet rays. Very few heat rays are emitted except the infrared wave-lengths, derived from the heating of the quartz container itself, and the metallic electrodes and the surrounding hood. It is interesting to note that, after 1000 to 1500 hours intermittent usage, little less than 50 per cent of ultraviolet rays are still present. The total radiation after the same period decreases in intensity one-half to one-third the initial value.

The reflecting mirrors employed in this series are made of quartz resting upon a nickel base. The surface is concave to obtain a greater intensity. Mirrors first tried were of solid quartz, surfaced with platinum. On comparing the intensity of chemical radiation emitted, it was found that too much was lost to make the latter valuable. These reflectors are attached to the water-cooled mercury quartz light (Kromayer lamp). Laryngeal reflecting mirrors can also be employed with the air-cooled lamp, but the intensity of radiation is reduced too considerably to make it serviceable.

As far as was ascertainable, all workers thus far have employed reflected radiation, each aiming by some special means to obtain the greatest ultraviolet intensity. A direct source of radiation which the new lamp offers would seem more desirable. The lamp is a small mercury quartz water-cooled apparatus, similar to the Kromayer lamp, which can be easily handled and is not too large for insertion into the mouth. The top is covered with silver-leaf, so as to prevent burning of the pharynx and to obtain added reflection. Applied to the skin, radiation from this source produces, with a two minute exposure at a distance of two inches, a marked erythema. The lamp is curved to conform to the pharynx and can be placed close to the larynx. The frequency and duration of the exposures depend upon the reactions obtained. The proper dosage for ultraviolet exposures of any lesion has not yet been accurately determined and must still be based upon experience. Actinometers, recently devised by Fürstenau and others, and consisting chiefly of selenium cells, have not yet proved their value. It has been shown by many that with the X-ray, both for superficial and deep lesions, minute radiations can produce stimulation, while larger doses can easily destroy tissue. This would similarly seem to hold true for any form of light rays, the change occurring with only the smallest variation in dosage. We can provide either activation with small exposures or destruction with larger ones, a fact that has been demonstrated by Hess with the epithelial cells of the capsule of the lens, by Bovie with unicellular organisms, by Behring and Meyer with ferments and by Lutz with cells of the epidermis. Hence it is obvious how necessary it becomes for us to develop some means of accurately dosing our radiations, a measure that is for the present lacking. Until then, comparisons of results of different workers will be difficult.

What is known of the direct effect of light rays upon tissues? The heat rays (red and infrared) set up an immediate vascular dilatation. This hyperemia interferes with the penetration of the ultraviolet ray, as

Finsen has shown, but may nevertheless prove a factor in stimulating healing. The penetrating power of the heat ray is great.

The actinic rays (blue, violet and ultraviolet) produce chemical changes. The hyperemia set up by them occurs only after a latent period. Their irritating power may stimulate response on the part of an otherwise sluggish disease process. It is doubtful whether these rays have a specific selective destructive action upon tuberculous tissue. They can however rapidly destroy tubercle bacilli, but this bactericidal effect plays a minor part, if any, in the healing of lupus, as Klingmüller and Halberstädt have shown. Finsen at first wrongly considered this the essential factor but his pupil Bang emphasized the hyperemic effects. It was Finsen who demonstrated that the chemical rays were those producing healing. Krüsius, with sunlight, was able to delay the development of experimental corneal tuberculosis in rabbits by exposure made immediately after inoculation, and considered this due to the destruction of some of the inoculated bacilli. According to Browning, Russ, Bovie, and Schunck, the bacteria are particularly affected by the shorter ultraviolets, those wave lengths not present in the solar spectrum as it reaches the earth.. The ultraviolet rays are most easily absorbed in the superficial layers of tissues and it is this marked absorption that brings about the chemical changes. This is the factor generally emphasized as very important for healing. The violet, indigo and the blue rays have a somewhat deeper penetration.

The tissue proteins are easily acted upon by the shorter ultraviolet rays, whereby albumins become globulins; the protein of tuberculin can be affected; and movements of colloidal particles cease. Ferments are affected (Neuberg and Packard); and peroxidases can be increased by small doses of the longer actinic rays, but destroyed by larger doses of the shorter ultraviolet wave-lengths (Behring and Meyer). Lymphocytes can be increased by local exposures of the shorter ultraviolets (Janet Clark).

Histological changes after ultraviolet exposures of tubercles of a rabbit's cornea (Jansen) show destructive effects, namely dilated vessels, partial thrombosis and destruction of giant cells and epithelioid cells, followed by a serous and serofibrinous exudate, with a collection of white blood cells, and finally vacuolization and necrosis. In lupus, there were fewer blood vessel changes because of lessened vascularity. Jansen could find these effects no deeper than one-half millimetre.

To increase the direct effectiveness of ultraviolet radiation upon tissues, fluorescent substances have been applied in isolated instances to the larynx. In this way, it was hoped that greater penetration of the shorter actinic rays could be brought about. The results were not encouraging. I attempted this with eosin applications upon five patients but discontinued it because of the lack of encouraging results. It might be better to apply quinine rather than eosin with ultraviolet wavelengths, as the absorption spectrum of quinine is best for the ultraviolet rays. However its disagreeable taste prevented me from using it.

Have we a right to expect unusually rapid healing in the application of an intense source of ultraviolet radiation to the larynx? Judging from the results obtained by Finsen with lupus of the skin, a superficial lesion to which direct pressure could be applied, it would not be probable. It generally required exposures of one hour every five days with the carbon arc over a period of six months or more to obtain healing in the lupus cases. With the reflectors employed in this series, the patients have taken exposures by graduated increase up to forty-five minutes biweekly, the duration being decided by the reaction. The mucous membranes withstand radiation fairly well. With the direct source of light, exposures thus far have been increased only to ten minutes. Some patients occasionally did develop burns in the pharynx, but these were never very serious.

Many workers have tried to heal disease of the larynx with general exposures of the entire body to ultraviolet radiation. Blegvad, Malström, Strandberg and other Scandinavian workers claimed good results with the carbon arc. Jesionek maintained that by general exposures he could obtain focal reactions in the larynx, but only in patients who had developed an intense skin pigmentation. Malström believed that he obtained them with general exposures of the carbon arc. The effect of general radiation upon the body tissues is not firmly established, but we can conceive of an indirect effect upon a distant focus of disease by way of the blood stream. How this occurs must yet remain unexplained. Changes of colloids and cell membranes, increased oxidation and reduction, changed proteins of the tissue cells and blood serum, variations in the number of blood cells, destruction or activation of ferments, have all either individually or collectively been held accountable. The good results with general radiation have not been realized by many workers other than the Scandinavians. It was tried upon ten of my selected patients, but with only little encouragement.

Blumenfeld considers that the principal factor in the development of a tuberculous laryngitis at the commonest sites of infection, namely, beneath the vocal cords and the mucosa of the posterior commissure, is the retardation of the lymph stream in these regions. It is interesting to note further that some observers have claimed, on the basis of theory only, that ultraviolet radiation aids by stimulating lymphatic flow. Should these assumptions have stronger foundation, one might be justified in offering ultraviolet radiation as a prophylactic measure at the very onset, when any sign whatsoever would make us suspect the larynx.

What evidence have we of the healing effect of direct ultraviolet radiation upon other superficial lesions? Cold abscesses gradually lose their suppuration and the clean wound is then stimulated to granulate. Fistulae are more difficult to heal, because of our inability to bring intense radiation to the very depths of the lesion. With nontuberculous, suppurating wounds, bacteria are quickly diminished; but reports do not agree as to the stimulation of granulations. Suppurating otitis media, tuberculous in character, can lose its discharge under these direct ray applications. Tuberculous keratoconjunctivitis heals similarly (Passow and Lundsgaard). Many other reports contradict these results but, here again, the difficulty of accurate dosage and the variations in application compel us to reserve judgment.

Before closing, a few general remarks upon the cases treated by me may not be amiss. Evidences of a marked focal reaction occasionally were noted by a feeling of fulness and dryness of the larynx; also pain and burning. Erythema and swelling, lasting about forty-eight hours, were seen in a few cases. With one patient a sharp red line of demarcation on the vocal cords was present, demonstrating the part that had been exposed and the part that had failed to be reached by the rays. One reaction occurred of marked intensity, with slight edema of the glottis and inability to phonate and swallow, which proved rather distressing for five days and then gradually subsided. Only afebrile cases were radiated, because the patients had to come to the office for exposures. There were no marked sudden changes, but most of those who took the radiations biweekly for over three months were bettered, and many of them had had a previous trial of silence treatment without result. Some ulcers healed but a few have not responded. Swellings were often diminished. Irritating cough disappeared at times. Three cases of dysphagia were relieved, but two did not respond without aid of drugs. No harm has been noted in any case.

CONCLUSIONS

1. Ultraviolet radiation heals superficial tuberculosis (lupus) but requires prolonged periods of time.

2. Important direct effects of ultraviolet radiation upon diseased tissues, namely, destruction of superficial organisms, production of hyperemia with chemical changes of cell protoplasm and special influence upon the ferments, are known.

3. Theoretically, one may justifiably expect that ultraviolet radiation, of sufficient intensity to produce focal reactions, can stimulate healing of tuberculous laryngitis.

4. Impressions thus far obtained by this form of treatment by direct application of the rays are encouraging.

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THE DETERMINATION OF CLINICAL ACTIVITY IN PULMONARY TUBERCULOSIS FROM ROENTGENOGRAMS

(A Preliminary Study)

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We have attempted to interpret X-ray findings in pulmonary tuberculosis not only with regard to the extent of the lesion, but also as to whether the character of the lesion observed might be associated with the symptom complex that one observes in pulmonary tuberculosis. Determination of activity in pulmonary tuberculosis in the minds of probably most phthisiotherapeutists is limited to symptoms and physical signs of the patient. Attempts to determine activity by means of complement fixation, tuberculin, auto-urine inoculation, chemical urine reactions, and sputum analysis have been made with unsatisfactory results. At the present time at the Trudeau Sanatorium clinical activity is based chiefly on temperature and pulse. A case is called active when a patient's pulse and temperature for more than three of seven consecutive days is above a rate of 90 and 99°F. for a male and above a rate of 96 and 99.6°F. for a female.

The object of this paper is to try to bring the interpretation of roentgenograms of the lungs to such a fine point that the observer can determine, without clinical information of the patient, whether activity or inactivity exists. For a determination of such sort we have a definite pathological background which one ought to be able to demonstrate in an X-ray plate. Clinically we see patients with great variation in the extent of their lesions, some having a very extensive process and classified as far advanced, others on the contrary with hardly enough to be called incipient. However, the former, who are expected to do badly, often do well and are without increased temperature and pulse, while the latter group may show all of the symptom complex which one finds in active pulmonary tuberculosis.

That a minimal lesion may give a greater symptom complex than a more advanced case has been attributed to differences in virulence of the infecting organisms or to a decreased resistance of one patient in comparison with another. However, another explanation might be advanced. The anatomical unit of tuberculosis is the tubercle. The first effects of the lodgment of the tubercle bacilli in the tissues are the destruction of the adjacent cells. By irritation both from the products of metabolism of the bacteria and from the action of foreign bodies the tubercle bacilli stimulate the surrounding tissues to proliferate a large quantity of epithelioid cells. This proliferation affects not only the connective tissue but also epithelial and endothelial cells of the vessels. An infiltration of leucocytes and lymphocytes takes place. The mass of epithelioid cells surrounds the tubercle bacilli. The cells increasing by cell division cause a pressure on the peripheral layers and produce a dense heaping up and flattening of cells at the periphery tending toward encapsulation of the tubercle. The included vessels are obliterated by a coagulative process. The epithelioid cells at the periphery change their form, elongate and become fibroblasts, and make their way into the mass from the periphery. As a result of this the tubercle becomes avascular. MacCallum states that there is no provision made for a blood supply in such nodules and those capillaries, which were present at that point before, are found to be obliterated, so that if an organ studded with tubercles be injected through an artery with blue gelatin each tubercle will stand out as a white nodule against a blue background. Whether the lymphatics bear the same fate as the blood vessels has been a much disputed question. Some authors claim that the spread of infection to the adjacent parenchyma occurs through these nonoccluded channels and that the substances that produce the toxemia are carried into the circulation through the same source. That the flow of lymph in the tissues is found to be exceedingly slow and that the flow of the lymph is dependent upon the pressure within the blood vessels are known facts. Therefore, inasmuch as the blood vessels in a tuberculous area become occluded, the flow of lymph from an area of that sort must be almost negligible.

As the tubercle becomes avascular, the toxins and endotoxins liberated by the metabolism of the bacilli and the disintegration of cells are no longer absorbed into the circulation. That nature at once infiltrates those areas which are infected by tubercle bacilli in order to cut down the circulation, that there will be as little absorption of toxins as possible, is apparent. Between the time of the infection and the time the lesion becomes avascular, we have a definite symptom complex and the degree of toxemia is not dependent on the size of the lesion but on the extent of lesion bathed by the circulation. We can now readily see that a patient with a vast amount of lung tissue diseased, which, however, because of fibrosis is shut off from the circulation, has no symptoms at all and apparently does well.

We may assume that the absorption of toxins is more likely to occur in the formation of new tubercles which are not walled off than the walled off fibrous and calcified tubercles. In fact, we may go a step further and assume that, inasmuch as we know that fibrosis has taken place, circulation in that area has ceased and therefore absorption of toxins from that area is not possible. Some investigators claim that depending upon the amount of fibrosis present, a proportional amount of diffusion of fluids exists between the tubercle and the adjoining living tissue. That this can be only small in amount if it does occur is apparent. Since circulation plays so great a part in toxemia we can see how easily the latter is dependent upon the amount of lesion the circulation drains. For example, two lesions of equal extent and intensity in one of which the tubercles coalesce and in the other disseminate give different pictures of toxemia. The area drained from the coalesced tubercles is small in comparison with the total area drained from the disseminated tubercles.

The pathological changes that may take place in tubercles will now be considered. The changes follow the death of the cells in the tubercles. A form of coagulation necrosis follows and the cells lose their outline and nuclei. This necrotic area is firm in consistency and may become stony through deposits of calcium salts. The area on the other hand may frequently soften because of secondary infection. New tubercles may often become hyaline and fibrous. When softening and caseation occur the necrosis may invade the adjoining normal parenchyma and spread from there by continuity, lymphatics, and blood supply. If the necrosed area extends through the wall of a bronchus, the contents are expelled into the lumen of the bronchus and expectorated.

If the cavity is small, granulation tissue may appear at the base and the cavity becomes gradually smaller and smaller, contracting entirely, and converted into a cicatrix. On the other hand, if the cavity is large an encapsulating membrane may occur between the cavity and the living tissues, the mouth of the cavity remaining open in the bronchus. This form of cavity is always a source of danger, as infectious material may be aspirated into the nonaffected areas at any time. Softening and necrosis at the visceral pleura may cause a spontaneous pneumothorax. When the interlobar pleura becomes involved localized pneumothoraces very often occur. The localized pneumothoraces are commonly seen as annular shadows and very often resemble cavity formation. Spontaneous pneumothorax and localized pneumothorax should be looked upon as the result of recent processes of softening.

An exact and precise description of the radioscopic appearance of the thorax is difficult and the added task of differentiating between activity and inactivity of a lesion even more so. Interpretation of shadows in roentgenograms should always be associated with the pathological process which may account for such shadows. Tubercles may occur in various stages—from early formation in which the tubercles are not walled off to the later stages in which they are fibrous and calcified (walled off tubercles). Shadows cast by tubercles vary almost directly in proportion to their density. Shadows cast by new tubercles are nebulous in character, and their margins appear to shade into the adjoining parenchyma, while a more opaque appearance with sharper margins of the shadows occurs with the fibrous and calcified tubercles.

Pulmonary changes created by the advance or retrogression, and, if we may say, final healing of pulmonary tuberculosis, produce certain shadows in the roentgenogram, which may be differentiated. Pathologically active tuberculosis differs materially from the healed tubercle or the resulting scar tissue. In the active cases we see an entirely different picture from that seen in the case which can reasonably be considered healed. In the former we usually see a combination of various shadow manifestations and in order to avoid confusion an attempt will be made to describe a small field in the active process. Assuming that there is no scar tissue or calcification in this limited area, we see mottling with decidedly ill defined margins, or a "cotton ball" appearance as we prefer to call it, blending gradually with the surrounding lung tissue, which appears hazy and cloudy. When the above picture can be demonstrated in the roentgenogram, we can be reasonably certain that both pathological and clinical activity are occurring.

Assuming that this cottony appearance indicates activity, as the disease retrogresses the lung tissue surrounding the "cotton ball" appears to become better aerated and probably at the same time we realize that the "cotton ball" is smaller and more compact. Or again, we may see the "cotton balls" (usually the small ones) almost fade from view, leaving a more or less finely dotted appearance or little string-like shadows.

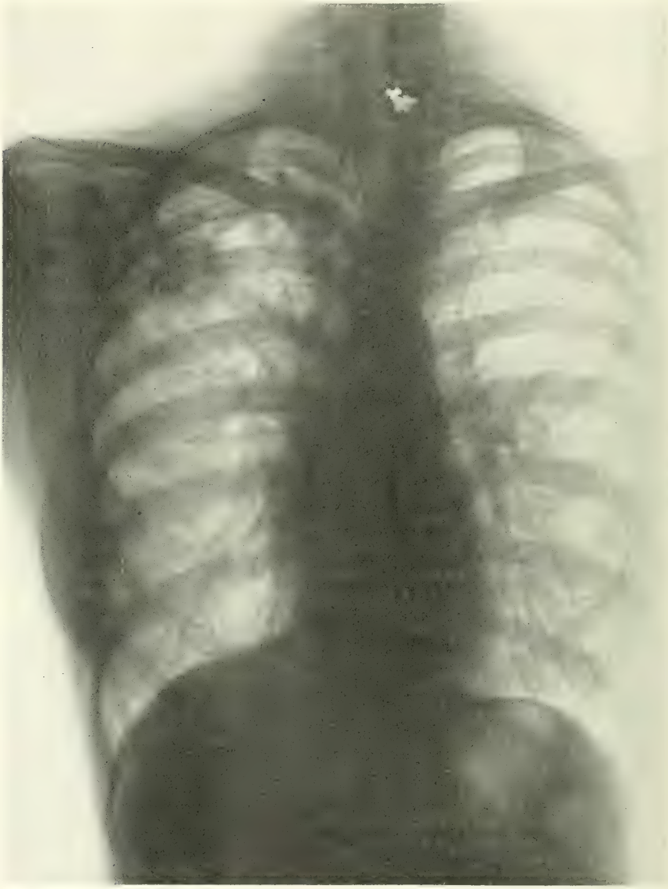

Fig. 1. Appearance of an Active Parenchymatous Lesion, Classified under Group XX

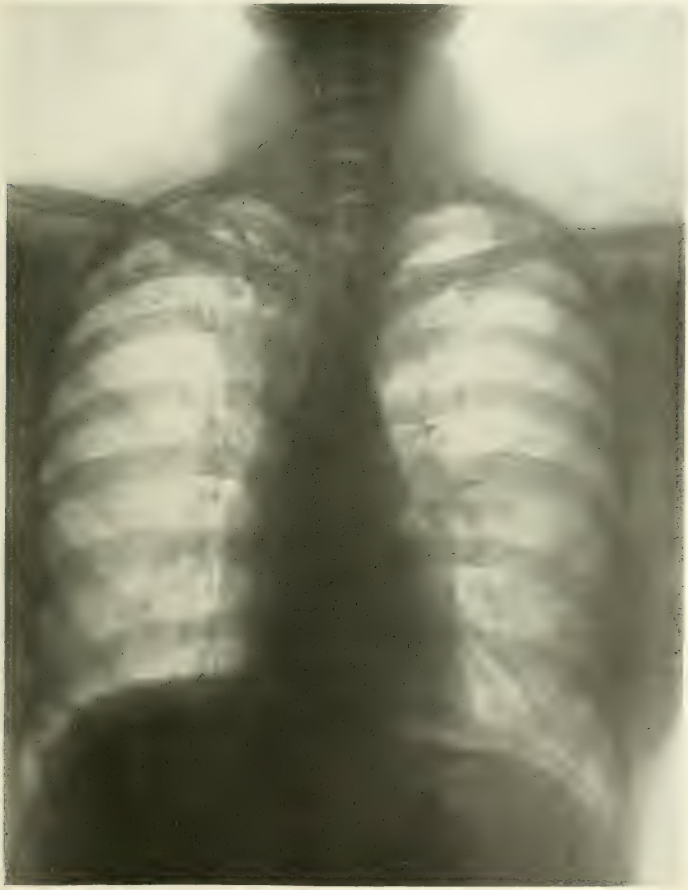

FIG. 2. THE SAME CASE AS IN FIG. 1, ONE YEAR LATER, SHOWING DEFINITE CLEARING, AND NOW CLASSIFIED UNDER GROUP X

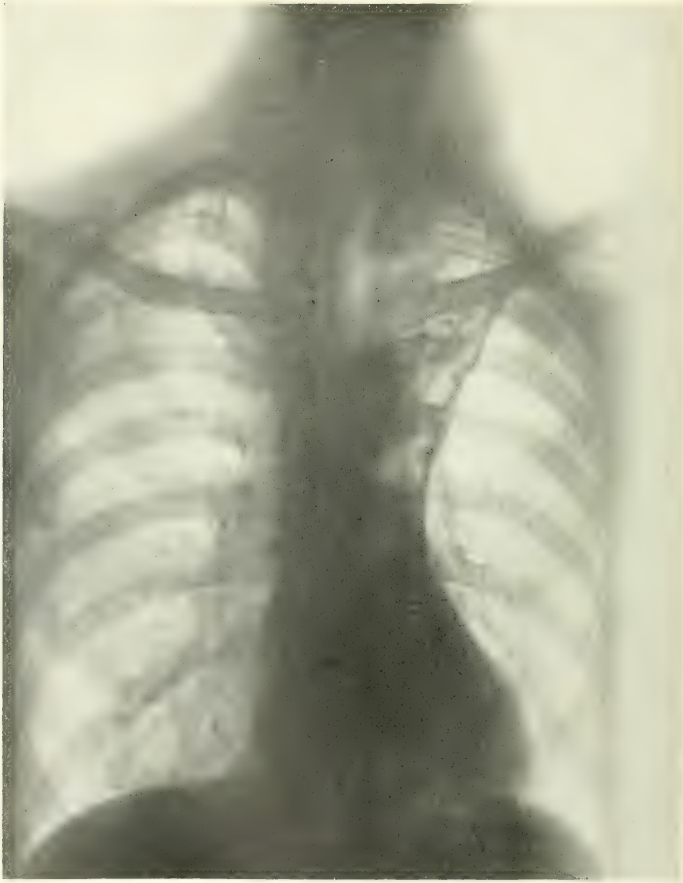

FIG. 3. PARENCHYMATOUS LESION, SHOWING MARKED FIBROSIS AND CALCIFICATION, CLASSIFIED UNDER GROUP *O*

As time goes on, when the patient is doing well, the mottling loses still more of its collateral haziness; the "cotton balls" become more compact or their appearance more discrete, the ray filtering through areas that were previously hazy; and the picture is that of a better aerated lung. As a rule, further retrogressive changes occur in this group and the patient is clinically inactive.

We have still another group of cases in which the plates show a preponderance of string-like or wiry shadows, or dense discrete mottling. In this group further retrogressive change is hardly possible and we may look upon these cases as probably healed tuberculosis.

From the above discussion of pathological changes in the lungs, their relationship to circulation and the X-ray evidence of these pathological changes, it is evident that unless there is an occurrence of new tubercle formation demonstrable in the roentgenogram as described above, even in the presence of extensive lesion one may conclude that, at the time of the reading, clinical activity is absent.

Our studies were based on one hundred cases. The stereograms were interpreted without any information of the cases, and placed in three groups, the first in which both clinical and pathological activity were present, a second group in which further retrogressive changes were probable, and in this group clinical activity absent, and a last group in which the condition simulated as closely as possible healed tuberculosis. The X-ray diagnoses are compared with the clinician's diagnoses of activity or inactivity. Out of one hundred cases, eighty-seven agreed with the findings of the clinician. Five cases called active by the clinician were diagnosed as inactive by X-ray. There were twenty-six cases that were diagnosed active by the clinician, therefore the X-ray diagnosed 81 per cent of the active cases. The course of the five cases was inactive. Out of seventy-four cases diagnosed inactive by the clinician, the X-ray diagnosed eight as active, that is, 88 per cent of this group were correctly diagnosed. The course in six of these eight was inactive. The course of the disease was, as a rule, the same as that of the X-ray diagnosis: these two agreed in 91 per cent of the cases.

SUMMARY

1. Activity is indicated in the roentgenogram by (1) mottling with decidedly ill-defined margins, blending gradually with the surrounding lung tissue, which appears hazy and cloudy (non-walled-off tubercles) and (2) the presence of spontaneous and localized pneumothoraces.

2. The amount of activity is dependent upon the area of surface drained by the circulation (coalesced or disseminated tubercles).

3. Diminished activity runs parallel to the amount of fibrosis and calcification that has taken place.

TUBERCULOSIS VERSUS INFLUENZA

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In the diagnosis of pulmonary tuberculosis it has become necessary to take into consideration many factors that were not considered essential several years ago. It was customary to make diagnoses based on the following essential points: a history of loss of weight, fever, cough, sweats, and exposure to tuberculosis. On physical examination the usual signs were changes in percussion note, changes in breath sounds, and râles in certain areas in the lungs. The roentgen ray examination of the chest by the fluoroscope and roentgenographic method showed evidence of densities in various parts of the lung, usually the upper. Whether tubercle bacilli were found in the sputum or not, the diagnosis of positive tuberculosis was usually made on the above findings. Since the epidemics of influenza in 1918, 1919 and 1920, there have been found many cases which fitted in very well with the cases formerly diagnosed as tuberculosis; but on closer analysis of these cases it was found that influenzal inflammation of the lungs gave factors similar in every way to cases of tuberculosis.

How then are we to distinguish these diseases when the signs and symptoms are so similar? It is the purpose of this paper to show the necessity of more careful analysis of signs and symptoms in lung cases, so that nontuberculous cases are not labelled tuberculosis, and vice versa. It is essential to recognize the fact that physical signs and roentgen rays are based upon the same physical factors, that is, densities in the lungs, produced by inflammation or new growth or congestion: all change the conduction of vibrations of sound and light in the same manner. It is therefore necessary to analyze the changes of sound and the changes of the roentgen rays in the light of the etiological factors.

Influenzal inflammation of the lung shows almost every variety of pathological condition in the lung that tuberculosis does. But time shows that the alterations in the lung do not remain constant as is usual in tuberculosis (1).

In case after case of so called tuberculosis, in which tubercle bacilli were consistently absent, serial X-ray plates and frequent examinations have shown the lungs to have regained their former condition. This does not occur in tuberculosis to such a degree. It is not unusual in tuberculous lungs, with bacilli, to find that the consolidation and shadows disappear to some degree; and it is well known that in the healing of tuberculous processes we have a shrinkage of the shadows due to the

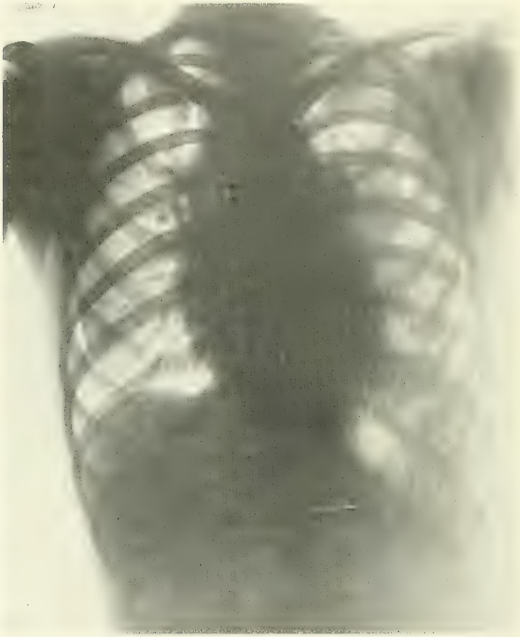

FIG. 1. ROENTGENOGRAPH TAKEN APRIL 28, 1920

The plate shows haziness throughout the left lung with a dense shadow in the 2nd, 3rd and 4th interspaces, partly connected with the hilum shadow. Lung markings at the apex are very much thickened and air content is not good. The left half of the diaphragm is raised high and there is no costophrenic angle. The right lung shows compensatory air content. The markings throughout the lung are thickened (probably hypertrophy of the lung tissue).

lessening of the congestion and the absorption of inflammatory substances.

I wish to report a case that has recently come under my observation which bears out these statements.

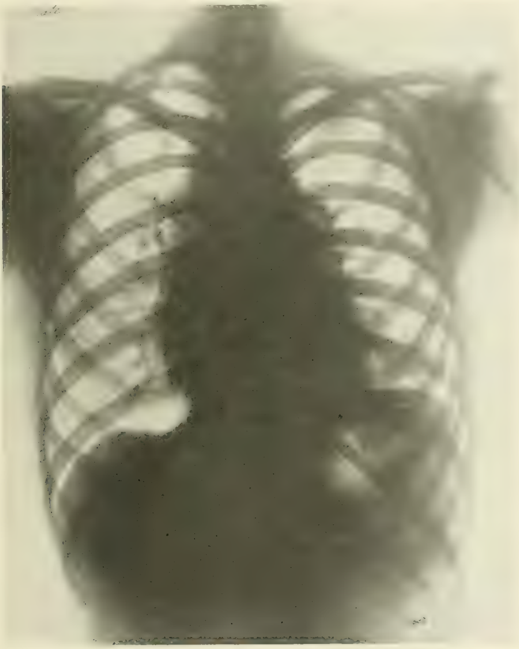

FIG. 2. ROENTGENOGRAPH TAKEN JUNE 5, 1920

The shadow in the 2nd, 3rd and 4th interspaces of the left lung, connected with the hilum, is rather dense, but is considerably less dense than in fig. 1. The air content is very much better. The left side of the diaphragm is still high and the costophrenic angle absent.

E.H., twenty-two years old, reported at the Washington University Dispensary, April 28, 1920, with a history of cough and pain in the left side. She had influenza two months previously and was confined to bed for two months. Since that time she has had cough and a feeling of general weakness. She had lost thirty-two pounds since January, has dyspnea on slight exertion, coughs a great deal, expectorates a great deal of thick purulent sputum, and has marked palpitation during coughing attacks. Her appetite is good, no nausea or vomiting, bowels and urinary condition normal. She has missed two menstrual periods since January. She feels drowsy and languid all the time. Her general health was good prior to January, 1920. She had whooping cough and measles, and influenza, lasting a week, one year before. Her habits were good and family history negative.

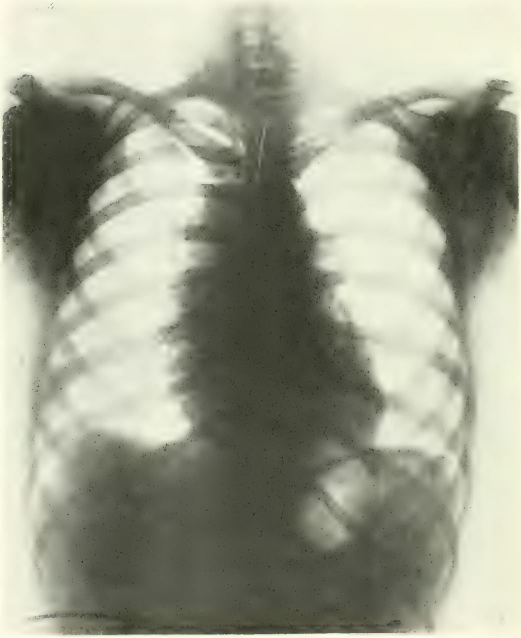

FIG. 3. ROENTGENOGRAPH TAKEN DECEMBER 2, 1920

The hilum shadow is perfectly normal, the diaphragm is still raised and the air content in the left lung is good.

Physical examination: Anemic young woman. Pupils equal, react to light and accommodation; teeth fair; small tonsils, which were congested; small thyroid; no other glandular enlargement. The physical signs of the chest show marked dulness throughout the entire left chest, both anteriorly and posteriorly. The breath sounds are diminished throughout the anterior area. The whisper and voice sounds are somewhat increased over the midportion of the lung posteriorly. There is an area, about the size of a dollar, at about the left angle of the scapula, where there is a marked increase of breath, voice and whisper sounds (positive D'Espine's sign). The base of the lung (left) posteriorly shows dulness, breath sounds and whisper almost absent. The right lung shows slight impairment at the apex, both anteriorly and posteriorly; below this there is compensatory emphysema. The roentgen ray plate at this time showed a definite shadow throughout the entire left lung, with a much denser shadow at the left hilum, about the size of a peach. The left diaphragm was high and the costal angle absent. The right lung showed slight haziness in the right apex with compensatory air; and a deep costophrenic angle. Her temperature was 99.2°; pulse, 120; weight, 113.

Upon these findings a positive diagnosis of tuberculosis was made, in spite of the fact that no tubercle bacilli were found. The patient was sent to the City Hospital for further observation, as she appeared too sick to be a clinic patient. On May 19, 1920, she returned to the clinic feeling somewhat better, and had gained three and one-half pounds with a marked improvement in her cough. The physical signs showed somewhat the same signs as the previous examination, but not so marked. The roentgen plate showed some clearing of the shadow in the left lung, except around the hilum which was still quite dense. In August, 1920, breath sounds were still diminished throughout the left chest. The roentgen plate still showed hazy shadows throughout the left lung. The patient had gained eighteen pounds and was working daily, but tired very easily. On November 27, she again returned. All signs had cleared up, except the increased whisper and slight impairment in the left posterior interscapular region. The roentgen plate then showed considerable clearing up of the shadow, except at the left hilum which was rather dense. On April 12, 1921, the patient returned weighing 161 pounds, a gain of 48 pounds. She feels perfectly well, has no cough and to all appearances is in perfect health.

In analyzing this case we have, then, definite history, physical signs and roentgen findings, all pointing to a diagnosis of tuberculosis; but in the light of the improvement, and the absence of tubercle bacilli and the changes in the roentgen plates, one feels that we had to do with a postinfluenzal inflammation of the lungs. It is now our custom to take serial plates of patients who show signs of tuberculosis, especially those in whom no tubercle bacilli were demonstrated in the sputum.

There has been a considerable literature on the subject of the relation of influenza to tuberculosis, from which a controversy has resulted as to whether influenza activates a latent tuberculosis of the lungs. A number of these cases of so called activated tuberculosis, I believe, are still postinfluenzal infections. The presence of tubercle bacilli is frequently the only deciding factor in the diagnosis of these cases.

In a recent paper Dr. Louis Boisliniere (2) mentioned a number of communications from various sanatoria. His conclusions were that a great number of cases of tuberculosis followed the influenza infection. Undoubtedly there are a great many cases of tuberculosis that developed after this infection, but great caution must be used if we wish to establish *definite* diagnosis. In conclusion I will say, that the "time element" in the diagnosis of tuberculosis following influenza is an important factor, and that several plates should be taken at various times in all suspicious cases, and repeated sputum examinations should be made.

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THE NUTRITION OF ACID-FAST BACTERIA

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Ever since the possibility of confusion has existed, those microorganisms which stain with more or less difficulty with the common aniline dyes, but which, once stained, retain their color tenaciously against acid and alcohol, have been considered as a biological division. About forty types, described at various times, have been herded together in bacteriological classification, largely on the basis of this single property, and spoken of as the "acid-fast" group, in distinction from such groups as the "colon-typhoid" group, the "mucosus capsulatus" group, and so on. Some of these are certainly identical, while others have been considered by many investigators as mutually transmutable, perhaps derived originally from a common acid-fast ancestor. More conservative writers (1), (2), (3) doubt this transmutability, however, and prefer to distinguish two main types, pathogenic and nonpathogenic, with several subgroupings within the two main divisions, based on habitat.

It would seemingly not be justifiable to classify these bacteria on the basis of that single attribute, unless it were a fundamental one not possessed by other bacteria and maintained always under given conditions by the ones in question. Reduced to concrete terms the propriety of placing them in a single group, since it cannot be done on the basis of virulence, depends, in the opinion of the author, upon the answer to such questions as these: Do they have in common any of the recognized chemical carriers of specificity? Particularly, do they possess common or closely related proteins not included in the bodies of other bacteria?—protein being generally considered the carrier of hereditary characteristics (4). Do they become non-acid-fast under any conditions and breed true in the new state? Can any of the bacteria outside the group be made to take on this property of acid-fastness? In summary, is acid-fastness a manifestation of any biological individuality?

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Now the nature and individuality of the proteins present in the protoplasm of different bacteria cannot be readily revealed by the present coarse methods of chemical analysis. Fortunately, however, we have most delicate tests of another kind, the so called biological ones, mysterious in their working, but none the less accurate, which permit a sharp differentiation of proteins. And on the basis of such tests we do have reason for believing that certain of the acid-fast bacteria possess common proteins not present in the bodies of certain other bacteria. The information is incomplete and will require much extension to furnish the basis for the formulation of a law, but it seems definite as far as it goes. Krause and Baldwin (5), who have reviewed the investigations of others, find in their own experience that guinea pigs sensitized with any of the following extracts: human type tubercle, butter, leprosy, timothy, milk, dung and smegma bacilli, will react to their proper antigen or to that of any of the others, but that none of the animals so sensitized will react to B. subtilis emulsion, nor will subtilis sensitized pigs react to the acid-fast preparations. On the other hand, Urbain and Fried (6) and others have noted a biological relationship between the tubercle bacillus and the diphtheria bacillus, in obtaining positive complement fixation with either bacterium as antigen in disease caused by the other. A situation of multiple antigen, somewhat akin to that discussed by Much, is quite naturally suggested.

Acid-fastness is most commonly explained as a function of the high wax content of these organisms. Yet it is far from likely that the wax itself is a carrier of any specificity (4). It is probably only associated with it, in which case it would be dependent upon some more significant underlying factor of nutrition. It should be mentioned that some non-acid-resistant saprophytic bacteria have been made to acquire acid-fastness by growth upon lipoid-rich media (7), and acid-fast ones to become non-acid-fast by cultivation upon media not readily adapted to the synthesis of fat (8).

Now a certain amount of specificity is unquestionably determined by the presence within a cell of a high concentration of a given enzyme (4). That statement altogether begs the question whether enzymes are proteins or not. A pancreas cell differs from a liver cell in the marked ability of its expressed juice to break down protein subjected to its destructive influence. It contains a high concentration of what we call tryptic ferment. A liver cell apparently differs from one of the intestinal mucosa in its faculty for working up the ammonia elaborated in the gastrointestinal tract into the innocuous substance, urea. Crudely expressed, these cells differ in one respect in that they work with different tools, more or less specific for each.

Bacteria, too, differ among themselves in the same way, and several good but incomplete classifications are based on the differences observed. The experiments recorded below represent a study of the similarities and differences in the action of the acid-fast bacilli upon some of the common food stuffs provided for them in nature. The attempt was made to learn whether they possess common nutritional properties as well as the compositional one expressed by the phenomenon of acid-fastness. No effort has thus far been made to trace their development from these foods. They were furnished with simple diets containing all the necessary elements for the construction of protoplasm, N, C, H, O, P, S, K, Na, Ca, Mg, and Cl; and they grew or died, according as they did or did not possess the tools for obtaining their livelihood from the materials in the form provided.

Nitrogen was furnished in certain well defined protein decomposition products, in amino, amide, amine and imino form. Carbon was supplied in the form of amino acids or certain alcohols and acids. P, S, K, Na, Ca, Mg, and Cl were kept constant in all experiments, the media containing 0.5 per cent NaCl, $\frac{N}{50}$ KH_2PO_4 and traces of $MgSO_4$ and $CaCl_2$. In addition, 2 per cent purified agar was used in all experiments except those with tubercle bacilli (human and bovine types). This may be considered an inert substance. Cultures were run in quadruplicate.

In the tables below growth is recorded by an arbitrary system of pluses, one plus meaning distinct but not heavy growth, two pluses, moderately heavy, and three pluses, profuse. Human and bovine type tubercle bacilli were grown for one month, and all others for two weeks. All were grown at 37°C. except the frog, fish and turtle bacilli, which were kept at 25°.

The isolation histories of the bacteria used were not known in all cases. H37 and R1 are old cultures of tubercle bacilli of the human type, isolated from cases of pulmonary tuberculosis seventeen and thirty years ago, respectively, the first of relatively high, the second of decidedly low virulence. H102 is a human type bacillus isolated from sputum in 1920. B1 is a bovine type bacillus isolated from a cow's lung in 1902. A1 is an avian bacillus isolated from a chicken in a California epidemic in 1905. The timothy bacillus and frog bacillus are descendants of

TABLE 1

*Growth on amino acids + 5 per cent glycerol**

AMINO ACID	H_{37}	H_{102}	R_1	B_1	A_1	A_2	LEPRA HARDY	LEPRA DUVAL	FROG	TURTLE	FISH	SMEGMA N. W.	SMEGMA S. L.	GRASS	GRASS III	GRASS IV	MIST	TIMOTHY
d-l Alanine	++	+	+	++	0	0	++	+++	+++	++	++	+++	+++	++	+++	+++	++	++
l-Alanine†	++			++	0	0	++	++	++	++	++	+++	+++	+++	+++	+++	+++	++
Leucine	+			+	++		++	++	++	++	++			++	++			+
Histidine	+				+	+	++	++	++	+	+							
Tryptophane	0			0	0			0	0	+	0		+	+	+			+
Phenyl alanine	0			0	+	+	0	0	+	0	0	+	+	0	+	0	0	0
Tyrosine	0	0	0	0				0	+				0					0

* In addition to $\frac{M}{10}$ concentration of the amino acid (except in the case of tyrosine, which was used in saturated solution) and the glycerol, each medium contained 0.5 per cent NaCl, M/50 KH_2PO_4, traces of $CaCl_2$ and $MgSO_4$, and was adjusted with NaOH to P_H 7.0.

† L-alanine was prepared by the method of Emil Fischer by benzoylating d-l alanine, preparing the brucine salts of the benzoylated compound, separating these by fractional crystallization, removing the brucine by alkali, and further purifying the l-compound through the strychnine salt. The strychnine was then removed as usual with alkali, and the resulting l-benzoyl alanine hydrolyzed with 20 per cent HCl to free the alanine. The possible racemizing effect of this last procedure cannot be ignored. The l-benzoyl alanine prepared as above gave approximately the same specific rotation as that observed by Fischer; the l-alanine obtained on its hydrolysis, very little rotation, if any. However, according to Fischer, optically active alanine has a very slight specific rotation, not nearly as great as its benzoyl modification. Under these circumstances I am not sure that I was using l-alanine free from the d-variety. It is usually stated that only the d-compound is biologically utilizable, although the evidence for this is incomplete. It will be seen in table 1 that the substance I used was readily utilized as a source of N when glycerol was present, and as a source of both N and C (table 2) when glycerol was absent, growth being not quite so good as with the synthetic alanine, which unquestionably contained 50 per cent of the d-variety.

TABLE 2

*Growth on amino acids without glycerol**

AMINO ACID	H_{37}	H_{102}	R_1	B_1	A_1	A_2	LEPRA HARDY	LEPRA DUVAL	FROG	TURTLE	FISH	SMEGMA N. W.	SMEGMA S. L.	GRASS	GRASS III	GRASS IV	MIST	TIMOTHY
d-l Alanine	0	0	0	0	0	0	+	+	++	++	++	++	++	++	++	++	++	++
l-Alanine					0	0	0	0	+	+	+	+	+	+	+	+	+	+
Leucine	0			0	0			+	++	++	++		+		+			+
Histidine	0				0	0	0	0	0	0	0	++	++	+	++	++	+	0
Tryptophane					0			0	0	0	0		0	0	0			0
Phenyl alanine					0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tyrosine	0	0	0	0	0			0	+				0					0

* See foot notes to table 1.

TABLE 3

*Growth on amino acids + glycerol.** *Effect of phenyl ring*

AMINO ACID	H_{37}	B_1	A_1	A_2	LEPRA HARDY	LEPRA DUVAL	FROG	TURTLE	FISH	SMEGMA N. W.	SMEGMA S. L.	GRASS	GRASS III	GRASS IV	MIST	TIMOTHY
$\frac{M}{10}$ alanine	++	++	0	0	++	+++	+++	++	++	+++	+++	++	+++	+++	++	++
$\frac{M}{10}$ phenyl alanine	0	0	+	+	0	0	+	0	0	+	+	0	+	0	0	0
$\frac{M}{20}$ phenyl alanine + $\frac{M}{20}$ alanine	+	+	0	0	0	0	+	+	+	++	++	+	++	++	+	+

* See foot note to table 1.

TABLE 4

Growth on amino, amide, amine, imino, and ammonia N (the medium contains glycerol)*

NITROGEN	H_{37}	H_{102}	R_1	B_1	A_1	A_2	LEPRA HARDY	LEPRA DUVAY	FROG	TURTLE	FISH	SMEGMA N. W.	SMEGMA S. L.	GRASS	GRASS III	GRASS IV	MIST	TIMOTHY
Alanine	++	+	+	++	0	0	++	+++	+++	++	++	+++	+++	++	+++	+++	++	++
Propionamide	+	++	+	+	+++	+	+	+	+	0	+	++	++	++	+	+	++	+
Ethyl amine (HCl)	0	0	0	0	0			0	+	0	0		0	0	++	++	0	0
Ammonia (HCl)	++	++	+	++	++	++		+	+	+	+		+	+			+	+
Creatinin	0			0	0	0	+	0	+	+	+	+	++	++	+++	+++	++	++
Urea	0			0	0		++	++	+	0	0	++	++	++	++	++	++	++

* See foot note to table 1.

TABLE 5

*Growth on ammonia + various substances containing carbon**

NUTRIMENT	H_{37}	H_{102}	R_1	B_1	A_1	A_2	LEPRA HARDY	LEPRA DUVAL	FROG	TURTLE	FISH	SMEGMA N. W.	SMEGMA S. L.	GRASS	GRASS III	GRASS IV	MIST	TIMOTHY
$NH_4Cl + C_2H_5OH$	0			0	0	0		0	+	0	0		+	+	+	+	+	+
$NH_4Cl + CH_3OH$	0			0				0	0	0	0		0	0	0	0	0	0
NH_4Cl + glycerol	++	++	+	++	++	++		+	+	+	+		+	+			+	+
NH_4Cl + glycol	0			0	0			0	0	0	0		0	0			0	0
NH_4 propionate	0	0	0		0	0	0	0	++	++	0	++	++	++	++	++	++	++
NH_4 acetate					0	0		0	0	0	0		0	0			0	0
NH_4 lactate	0	0	0	0	0	0	0	+	++	0	0	++	++	++	++	++	++	+
NH_4 glycollate					0	0	0	0	0	0	0	0	0	0	0	0	0	0
NH_4 pyruvate	0	0	0	0	+	0	++	+	++	+	++	+	++	++	++	++	++	++
NH_4 formate							0	0	0	0	0		+	0	+	+	+	+
NH_4 oxalate					0	0		0	+	+	+		+	+			+	+

* See foot note to table 1.

strains isolated by Moeller in Berlin about 1904. The turtle bacillus culture is the same as that brought to this country by Friedmann in 1913. The others are stock strains of some years standing from the American Museum of Natural History, and the Hygienic Laboratory and the Department of Bacteriology of the University of Chicago, for which exact histories were not available. All were acid-fast and remained so on all media used.

SUMMARY OF RESULTS

In table 1 growth with a number of amino acids as sole source of N and with glycerol as an additional source of C is recorded. These being all α-amino acids, the N has the same relationship to the rest of the molecule in each case: that one expressed by the formula $R. CH. NH_2. COOH$. R is either CH_3, as in the case of alanine, or CH_3 with one H atom replaced by another group. In all except leucine the replacing group is a ring structure. Table 2 records the availability of the factor R in its various forms for building the entire carbonaceous portion of the bacterial body, glycerol being left out of the medium, the remainder of the amino acid after the extraction of the amino group constituting the sole supply of C.

Summarizing the results obtained, we note that the amino group is utilizable by all bacteria as their sole source of N. With all bacteria used except the avian bacillus, alanine served readily as a source of N. Why alanine could not be used by avian bacilli, when isopropyl alanine (leucine) and imidazol alanine (histidine) were utilized, awaits later explanation. It is easier to explain why growth was relatively feeble when tryptophane (indol alanine), phenylalanine and tryosine (oxyphenylalanine) were used. These compounds contain the benzene nucleus, which in small amounts is toxic to bacteria. With each atom of N withdrawn, in the case of phenylalanine, for instance, a molecule of phenyl lactic or phenyl pyruvic acid is left as a possible interferent with growth, even when an adequate supply of C is available from another source, glycerol.

This factor of toxicity may be further studied in table 3. Three media were used for this experiment. In each case the same amount of N was present. In one medium was $\frac{M}{10}$ alanine, in another $\frac{M}{10}$ phenylalanine, and in the third $\frac{M}{20}$ alanine plus $\frac{M}{20}$ phenyl alanine, in addition in each case to 5 per cent glycerol. It will be seen that with the exception of the avian bacillus, for which an inverse relation obtains, as noted above, all bacteria grew well with alanine as a sole source of N, sparsely or not at all with phenylalanine, and that in the case of human and bovine type tubercle bacilli, turtle and fish bacilli, smegma and various types of grass bacilli, growth was improved by replacing half of the phenylalanine with alanine, but that such substitution did not restore growth to the level obtained with alanine in the absence of its phenyl modification. It is of course conceivable that bacteria use a different deaminizing enzyme for each amino acid, and that those studied here are better equipped with the one for alanine than that for phenylalanine, but it seems more probable that the factor concerned in the decreased growth with the latter is the toxicity of the compound left after the deaminization.

Table 2 shows the availability of the carbon residue left after deaminization. This residue seems useless to the tubercle bacillus in all cases, this organism being strongly glycerophilic. The leprosy bacillus on the other hand possesses the necessary tools for working up the residue from alanine and leucine, at least, into its own substance and maintaining itself on these residues as the sole source of its carbon. It is unable however to use the deaminized residue from histidine (from which it is able to abstract N: see table 1). Frog, turtle and fish bacilli behave in an entirely similar manner. In all probability we are dealing here with an inability to split the imid-azol ring of histidine into the simple groups from which synthesis of the necessary variety of bacterial building stones can start.

Smegma bacilli are better equipped for coping with an unfavorable environment, in that they possess the mechanism for deriving their entire carbonaceous nutriment from the imid-azol-propionic arrangement of C atoms, in all probability splitting the imid-azol ring. The same statement holds for most of the grass bacilli, the dung bacillus being considered a grass bacillus. Smegma and grass bacilli are however unable to get the necessary nourishment from the carbon residue of tryptophane, although, as table 1 shows, they are able to deaminize it. This means, either that they are unable to split up the indol-propionic grouping, or that the latter is too toxic. Probably the former possibility is the correct explanation, in view of the fact that some growth does take place when glycerol is supplied as an additional source of C, none at all occurring on tryptophane alone.

In table 4 a comparison is made of the utilization of N in various forms, amino, amide, amine, imino, and ammonia. In each case an adequate supply of C was presented in glycerol. Summarizing, we note that the amino group of alanine is readily used by everything except avian bacilli. The acid amide group of propionamide is used by all bacteria except the turtle bacillus. The ammonia grouping serves as the sole source of N for any of them, and it is probably chiefly by conversion into this form that the N of any chemical grouping is used. Creatinine is not used by tubercle bacilli, may or may not be used by leprosy bacilli, but is susceptible to the action of the bacilli of cold blooded animals, the smegma bacilli, and the various grass bacilli. It is an example of nitrogen in the imino grouping, vulnerable apparently to the above named group.

Urea, which may be looked upon as the diamide of carbonic acid or as the amide of carbamic acid, is not so readily utilized as might be expected. Readily available to leprosy bacilli, smegma bacilli, and all the grass bacilli, its N cannot be used by human, bovine or avian type, tubercle bacilli or by any of the bacilli of cold blooded animals except the frog bacillus.

Of all the bacteria used, only three possessed the power to use the N of ethyl amine. Curiously enough these were of different groups, two of them being grass bacilli, the other the frog bacillus. Tubercle bacilli were unable to utilize it. This experiment was repeated several times in view of the fact that two years ago the author (9) reported utilization of amine N by tubercle bacilli. As prepared, the amine used at that time must have contained some ammonium chloride, enough to account for growth of the tubercle bacillus. The product used in the experiments here recorded was ammonia-free, and it can be definitely stated that H37, B1, and A1 do not use this compound. In general the amines are stable compounds in the laboratory. The remarkable thing is not that so many bacteria failed to use ethyl amine nitrogen, but that some were able to do so. The frog bacillus and grass III and IV obviously possessed something lacking in the other bacilli, a mechanism for prying the NH_2 group off from a primary amine. No explanation can be given of the difference in the behavior of the frog bacillus and its supposed relatives, the turtle and fish bacilli, and in that of grass III and IV and the other grass bacilli. It was sharp and unquestionable, however, serving to show how complicated the problem of differentiating bacteria on a chemical basis may be. As a point of interest it may be mentioned that a culture of the frog bacillus contaminated with B. subtilis was readily cleared of the contamination by growth upon an amine medium, in which ethyl amine was the sole source of both N and C, B. subtilis being unable to use the amine.

The action of the frog bacillus was further examined in the following experiment. Fifteen bottles of a medium containing ethyl amine hydrochloride as the entire supply of N and C, after serving for the growth of the frog bacillus for one month, were distilled, and the distillate was treated with ammonia and Lugol's solution. No crystals were formed, but a marked odor of iodoform developed, indicating the production by the frog bacillus of a certain amount of either ethyl alcohol or acetaldehyde in the medium. A control of fifteen bottles inoculated at the same time with the grass bacillus, which did not utilize this compound, was subjected to the same treatment and failed to give the test.

In table 5 is indicated the utilization of C in various forms, from which only empirical deductions can be drawn at the present time. Glycerol is readily used by all members of the group. Glycol, its homologue with one less carbon atom, is not utilized by any. Ethyl alcohol has a limited utilization, serving as a sufficient source of carbon to the frog bacillus, smegma bacillus and grass bacilli, and perhaps some of the others not tried. Methyl alcohol, its homologue with one less carbon atom, is unutilizable. So much for alcohols. Propionic acid served as a complete source of carbon for frog, turtle, smegma and grass bacilli, but not for tubercle, leprosy or fish bacilli. Its homologue with one less C atom, acetic acid, was unutilizable. Lactic acid was similar in its nutritive value, except that the leprosy bacillus did use it and the turtle bacillus did not. Its homologue with one less carbon atom, glycollic acid, was unutilizable. Pyruvic acid sufficed as sole source of carbon for all bacteria except human and bovine type tubercle bacilli and one of the avian strains. Its homologue, glyoxylic acid, was unfortunately not available for investigation. Most remarkably, for some bacteria formic and oxalic acids could serve as the sole source of carbon. These substances contain only H_2 as available energy; unknown reduction processes go on to render their carbon utilizable.

In general, it will be noted from the above summary that the three carbon atom acids are utilizable for synthesis, and the two carbon ones not. It is to be noted that the alcohol related to the three carbon atom acids in sugar metabolism, equivalent to lactic acid minus carbon dioxide, namely, ethyl alcohol, is utilizable, while the alcohol similarly related to the two carbon acids, methyl alcohol, is unutilizable. The usefulness of glycerol and nonutility of glycol for this group of bacteria is no new observation, it having been recorded years ago by Proskauer and Beck (10).

DISCUSSION

The protocols above record the results of some four hundred and fifty culture experiments, or about eighteen hundred cultures, since each experiment was carried out in quadruplicate. Naturally, in a series of that size many discrepancies occur. Space would not permit a separate discussion of all of these, nor would such discussion, indeed, be profitable. We cannot ignore the fact that bacteria as living things possess a certain variability not encountered in standard, dead chemical reagents. I have seen a chromogenic strain of grass bacillus run pure white through three weeks on one transplant in quadruplicate and return to a bright yellow in the transplant from this to the same medium. It is no cause for wonder that their chemical action on food stuffs is not always as expected.

In spite of this fact and in spite of the fact that the above tables are obviously incomplete, various strains being added or withdrawn in the course of the investigation, perhaps enough broad generalizations may be drawn from them and the summaries given in the text, to furnish a start on classification, subject always to revision. Furthermore, if this classification is to be useful in a practical way, it must recognize the point of view of parasitism as against avirulence.

One of the characteristics of saprophytes as seen in the uncontrolled conditions of nature, is their ability to break down very complex into simple compounds, from which new life is constructed, the familiar organic decay, which constitutes an arc in the great carbon and nitrogen cycles. Complex chemical groupings such as the benzene and indol rings are torn to pieces, the imino grouping is vigorously attacked by saturation with water, and ammonia is pried loose from stable things like amines. In a general way parasites are more helpless, and more likely to thrive on nutriment a portion of which at least is predigested, and many of them are prone to leave untouched difficultly digestible morsels like the aromatic rings. Numerous exceptions to these propositions can of course be cited, but they approximate the truth closely enough to be useful.

It will be noted in table 5 that the alcohols other than glycerol, and the organic acids used, are insufficient sources of carbon for the tubercle bacilli. They must have something more, preferably glycerol. They are thus at once set apart from the rest of this heterogeneous group, which use these substances to a varying degree. Turning now to some of those characteristics of saprophytism just mentioned, we note that the complex imid-azol-propionic structure (histidine) is utilizable by smegma and grass bacilli as a source of carbon and useless to the others. Something like the same separation can be made on the basis of the utilization of the nitrogen of the complex tryptophane (table 1). Utilization of the creatinin imino nitrogen and abstraction of nitrogen from urea again place the smegma bacilli with the grass bacilli and both of them apart from the tubercle bacilli. By exclusion of these two extremes, we have left the leprosy bacilli, provisionally so called, with due recognition of their insecure etiological status, and the bacilli of cold blooded animals. In their utilization of the carbonaceous portions of d-l alanine and leucine, these behave somewhat alike and more like the grass and smegma bacilli than like the tubercle bacilli. In their less general utilization of propionic and lactic acid and ethyl alcohol as sources of carbon, they act more like the tubercle bacilli. In their action on creatinin they are again more like the grass bacilli. In their failure to use the carbonaceous part of histidine they behave similarly and resemble more the tubercle bacilli.

From the above considerations it will at least be seen that the tubercle bacilli on the one hand and the smegma and grass bacilli on the other, fall rather readily into separate nutritional groups. The lepra and cold blooded animal bacilli have many points of difference from both of these and certainly a few nutritional factors in common. Tentatively they can perhaps be considered together as a third group. Finally it should be added that the distinction between human and bovine type tubercle bacilli has so far proved too subtle to be drawn on a nutritional basis.

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THE DIETARY REQUIREMENTS IN PULMONARY TUBERCULOSIS

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For a long time the conception of tuberculosis expressed by the popular term "consumption" has been the dominant one in determining the management of diets of phthisical patients. The rapid wasting, so characteristic of the disease, in the absence of certain knowledge as to its cause, was attributed to an abnormally rapid utilization of food and a consumption of body tissues in lieu of adequate amounts of food. It was but natural that one of the chief methods for combating the disease should have been a vigorous attempt to overfeed the patient. For some time, however, it has been evident to careful clinical observers that a regimen of overfeeding is not without danger and that it is frequently followed by disastrous results. In 1908 statistical data from many sanatoria, compiled by Irving Fisher (1), showed the wide variation in the practice of physicians as regards the dietary in pulmonary tuberculosis. Since then, undoubtedly, the custom of overfeeding phthisical patients has declined, yet it is still probably very common outside the larger sanatoria.

In 1919 it was decided to apply to this dietetic problem the methods of study of normal nutritional requirements. The first step was the actual measurement of the heat production of tuberculous patients in the Russell Sage calorimeter (2), to which data further observations made with a Tissot spirometer have been added. In this way it was possible to secure accurate information as to the actual amount of energy transformed by such patients in twenty-four hours, when at rest in bed. It was found that during afebrile periods the heat production was practically normal, according to the existing standards relative to height, weight, age, and body surface area. As the temperature of the body rose there was found to be a variable increase in metabolism, which in general amounted to 30 per cent when the rectal temperature was 104°F. (about 40°C.). It was noted that coughing and dyspnea lead to additional expenditures of energy. A still further increase in heat production is due to the specific dynamic effects of the foodstuffs ingested, which is most marked in the case of protein (3). From the data obtained from 21 cases of active tuberculosis studied, the twenty-four hour basal heat production varied from 1350 to 2030 calories.

One might estimate the probable energy requirement of such a patient, at rest in bed, somewhat as follows:

1. Calculate the twenty-four hour heat production for a normal individual of the same sex, age, height, and weight. For this purpose one may use either the formulae of DuBois (4) (5), which is the method used by us, or the prediction tables of Harris and Benedict (6). The two methods give essentially the same results.

2. Having estimated the basal heat production, if the afternoon temperature reaches 104°F., and if the patient has fever for only half the day, an increment of 15 per cent is added. If coughing is moderately severe, 5 per cent may be added. The usual allowance for the specific dynamic action of food, with ordinary mixed diets, is 10 per cent. When such calculations were applied to the individuals studied by us, the daily energy requirement was found to range from 1760 to 2640 calories while at absolute rest in bed, depending on the size of the individual and intensity of the febrile condition.

Pulmonary forms of tuberculosis present a peculiar problem from the standpoint of the metabolism, which depends for its maintenance upon the respiratory functions of the lungs. Anything that increases the metabolism requires that the lungs furnish a greater oxygen supply to the blood for the tissues, receiving in turn from the blood a greater amount of carbon dioxide for elimination. This increased exchange of respiratory gases involves the breathing of greater volumes of air, which is accomplished either by increasing the rate of respiration, or by increasing the depth, or both.

One of the earliest manifestations of pulmonary disease is the reduction of the vital capacity. As the vital capacity becomes smaller, the limit to the amount of tidal air becomes proportionally reduced, so that in advanced cases the demand for an increased ventilation of the lungs must be met entirely by increasing the rate of breathing rather than the depth. The diminution of the vital capacity is probably in part due to reflex inhibition of the respiratory movements, and in part to adhesions, infiltration, and increased vascularity. In so far as it tends to prevent the distention of diseased alveoli, before the tissue barriers to the disease are firmly established, it may be regarded as a protective mechanism.

In view of these facts it seemed wise, therefore, to select such a diet as will make the least demand upon the respiratory mechanism. For this reason a study was made of the effects of the ingestion of the various foodstuffs upon the breathing volume (3). The effects of food ingestion on the metabolism has been extensively studied by Rubner and Lusk. As regards the effect upon the heat production in tuberculosis the results obtained were quite comparable with those obtained in normal individuals. The greatest increase in heat production occurs in the case of protein, next, fat, and least of all with carbohydrates. Rubner found 5.8 per cent of the energy of ingested glucose appeared as the energy of specific dynamic action. For fat he found 12.7 per cent, but Magnus-Levy found only 2.5, and Murlin and Lusk found 4.1 per cent (7).

With protein and fat the effect upon the breathing volume is proportional to the effect upon the heat production. With carbohydrates the increase of breathing volume is large, and out of all proportion to that of metabolism. This anomaly is due to the fact that when the carbohydrates are metabolized the carbon dioxide elimination is greatly increased, although the oxygen consumption and heat production are but slightly altered.

As an example the following may be taken:

One hundred grams of glucose and 40.4 grams of fat yield about 375 calories in the metabolism. One hundred grams of glucose yield 146.6 grams of carbon dioxide on oxidation, whereas 40.4 grams of fat (tripalmitin) yield 112.5 grams. For one unit of heat produced from glucose there is a production of nearly 30 per cent more carbon dioxide than would have been evolved if the same energy had been obtained from fat. This carbon dioxide would necessarily act as a respiratory stimulant increasing the volume of the respired air. This effect would be superimposed upon any increase in the volume of respiration derived from the extra metabolism, due to the specific dynamic action of the foodstuff itself. The ingestion of 100 grams of cane sugar has been observed to increase the pulmonary ventilation 60 per cent (8).

The ingestion of 70 grams of protein was found to increase both the metabolism and ventilation about 25 per cent (2) (3). The ingestion of 1302 calories (140 grams) as fat produced an increase of only 12 per cent. The greatest number of calories may be obtained from fat with the least effect upon the volume of respiration. This is an interesting experimental confirmation of the correctness of the older clinical writers, who on empirical grounds urged the importance of fat in the diet.

In the first report of our studies (2) attention was called to the large specific dynamic action of protein, and the suggestion was made that it might be well to limit the protein of the diet during the periods of activity of the disease, in order to keep the breathing volume as small as possible. An investigation was made to determine the smallest amount of protein which would maintain nitrogen equilibrium in tuberculosis (9). In some cases it was possible to maintain nitrogen balance, and even to retain nitrogen, when from 37.5 to 43.8 grams of protein were ingested. The attainment of nitrogen equilibrium with such a small amount of protein was dependent upon the ingestion of large amounts of carbohydrate and fat, sufficient to make the total caloric value of the diet from 1.7 to 2.4 times the energy requirement, as calculated from data of basal metabolism determinations. It will readily be seen that such diets would not be economical from the standpoint of pulmonary ventilation, for though the heat production were increased but little by the protein the breathing volume would be greatly increased by the large amount of carbohydrate required.

When diets were given containing from 60 to 90 grams of protein, positive nitrogen balance was achieved with a total caloric value of less than 1.7 times the energy requirement of the basal metabolism. When the protein of such diets is divided between three or four meals the specific dynamic effect is almost negligible. If the patient tolerates fat well, a diet may be taken which involves very little increase in respiratory function. It seems, therefore, that the optimal amount of protein is between 60 and 90 grams.

It is well to emphasize the facts which have been demonstrated by Pearce (10), that not only the pulmonary ventilation varies with the metabolism, but that the circulation rate through the lungs varies in a similar manner. The observations of the effect of food upon the metabolism become doubly significant when we are dealing with pulmonary cases with hemorrhage.

A discussion of the diet in tuberculosis would be incomplete without mention of the mineral requirements. Balance experiments have been carried out by us, in which the simultaneous behavior of calcium, magnesium, phosphorus, and nitrogen excretion was observed. These experiments are very difficult to interpret, and for that reason will not be published until more data are obtained. Previous workers have held, on rather meagre evidence, that there is a decalcification in tuberculosis. As far as our own results are concerned, they seem to confirm the view that more calcium is required for the maintenance of equilibrium in tuberculosis than for normal men. This statement should be taken with caution and with reservations, until further work is done. Sherman (11) believes 0.45 gram per diem to be the minimal quantity of calcium for normal men. There can be no harm in giving two or three times this amount daily in the diet. It is readily available in milk, or by the administration of a calcium salt such as the lactate.

The steps by which our conception of the dietary requirements in tuberculosis have developed may be summarized as follows:

1. Estimates of the total daily energy requirements of patients have been arrived at by determination of the basal heat production, making suitable additions for the effects of fever, food ingestion, and of coughing upon the metabolism.

2. The difficult question of deciding upon the proper proportions in which the foodstuffs, protein, fat, and carbohydrate, should be combined, has been approached by a consideration of the close interrelation of the metabolism with the respiratory and cardiac functions. The aim has been to devise a diet, which will increase as little as possible the volume of respiration and the circulation rate through the lungs, in order to limit the functional demands upon an injured organ.

a. High protein diets greatly increase the metabolism and consequently enlarge the demands upon the cardiorespiratory mechanism. They produce undesirable effects upon the digestive and excretory systems as well.

b. While nitrogen balance may be attained on a low protein diet, this is only possible when the protein metabolism is spared by an excessive ingestion of nonprotein food, chiefly carbohydrate. The effect of a carbohydrate-rich diet is to increase greatly the breathing volume. Fat, which is metabolized with the greatest economy of respiratory function, is not so efficient as carbohydrate in sparing protein. Most individuals have a limited capacity for utilizing fat. If fat is well tolerated, however, it is well to keep in mind the necessity of maintaining a sufficient supply of carbohydrate to prevent the development of acidosis. Shaffer (12) has collected evidence to show that one molecule of glucose is necessary for the complete oxidation of acetoacetic acid, or one molecule of any higher fatty acid or amino-acid which yields one molecule of acetoacetic acid in the metabolism. Woodyatt

(13) has explained the methods of calculating the balance between the ketogenic and antiketogenic factors in a diet. Using his methods one finds that diets furnishing about 2500 calories, 60 to 90 grams of protein and 200 grams of fat, would require about 100 grams of glucose or other carbohydrate to maintain Shaffer's ratio. In this case about $\frac{1}{6}$ of the total calories would be derived from carbohydrate. It would be well to set $\frac{1}{5}$ of the total calories as the minimum for the proportion of carbohydrates in the diet.

c. Satisfactory nutrition may be attained by the use of moderate quantities of protein (60 to 90 grams per diem), with the use of fat up to the limits of digestive capacity, and sufficient carbohydrate to bring the total caloric value of the diet to from 2500 to 3000 calories. Such a diet will produce the least demand upon the function of the damaged lungs. From the standpoint of diminishing the specific dynamic effects of foods, there is an advantage in dividing the diet into more than three meals.

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THE INTRAVENOUS INJECTION OF CALCIUM CHLORIDE IN THE TREATMENT OF INTESTINAL TUBERCULOSIS

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That there has been no problem more baffling to the phthisiotherapeutist than that of the early diagnosis and treatment of intestinal tuberculosis, is a statement that will not be generally denied, and those of us who have occasion to see much of tuberculosis, especially of its enteric form, have hitherto felt a pessimism as to its cure that has been only too well justified.

Those tuberculous patients who complain of indefinite digestive disturbances have usually been treated for dyspepsia, though too often they later showed symptoms so marked and persistent that a diagnosis of intestinal involvement was forced upon us. Yet even then we had no positive means of assuring ourselves of the correctness of our suspicion diagnosis until the palpation of a thickened cecum brought certainty, for bacilli in the stools are generally recognized to be an inadequate basis for diagnosis.

Empiricism in medicine is always to be regretted, but an empirical remedy that is of aid to the patient, while it may not satisfy our desire to comprehend its workings, is nevertheless more valuable than one based upon sound scientific principles, but accomplishing no good. The administration of calcium chloride in tuberculous diarrhea is, we believe, based on empiricism, but of its good effects there are at present many undeniable examples. It is our purpose briefly to set forth our results obtained in the treatment of thirty cases of tuberculous diarrhea by the more or less frequent injections of from 5 to 10 cc. of a 5 per cent calcium chloride solution.

A word as to the nature of our cases. We have taken them as they came; and in many instances calcium chloride was used with no hope of beneficial results, but merely to try to give these unfortunates some relief. In a practice devoted mainly to the treatment of pulmonary tuberculosis, we naturally see intestinal involvement as a late development and frequently as a terminal phase. Thus in all but eight of our cases (1, 8, 11, 15, 18, 23, 26, and 28) pulmonary involvement was very great. In sixteen cases (2, 5, 6, 9, 10, 12, 13, 16, 17, 19, 20, 21, 22, 27, 29 and 30) it was so extensive as to preclude any possibility of recovery whether the intestinal condition became ameliorated or not. In two cases (11, 15) the diagnosis of tuberculous diarrhea was very questionable. We have used calcium chloride, of course, in no sense as a curative agent, but merely as a palliative in an attempt to control the distressing symptoms of pain and diarrhea.

In our work we have administered calcium chloride invariably by the intravenous route. We have no comment to make on the technique of injection, as it is in every way similar to the intravenous injection of any small quantity of fluid, save that great care must be taken that none of the solution escapes into the subcutaneous tissue, as it is very irritating, causes excruciating pain, and may set up an area of necrosis and gangrene. We have had but one severe reaction following injection, but we have always been careful to inject the solution very slowly indeed. A goodly percentage of the patients noted a strange feeling of heat, beginning in the throat and rapidly extending over the entire body; this sensation becoming evident after the injection of as little as 1 cc. of the solution. Two or three times, patients have complained of a feeling of faintness, but they were of the nervous type and would probably have reacted thus to any intravenous injection that necessitated a little time in its administration. We were never able to persuade ourselves that their feelings were in any way related to the calcium chloride as such.

We have not adopted any definite interval between doses but have gauged the frequency of injection by the clinical symptoms. In the few patients to whom we have administered the drug over a considerable period of time, we have gathered the impression that by continued and repeated use, it loses some of its efficacy, and as time goes on holds the symptoms in check over a gradually lessening interval.

Table 1 shows the results we have obtained, and we propose now briefly to discuss a few of the most characteristic cases.

Of these thirty cases, one received fifty-two injections (no. 1), one received fifteen injections (no. 18), one received eleven injections (no. 16), one received seven injections (no. 8), one received six injections (no. 26), two received five injections (4 and 25), two received four injections (28 and 29), two received three injections (17 and 20), sixteen received two injections (2, 3, 5, 6, 7, 9, 10, 13, 14, 19, 21, 22, 23, 24, 27, 30)

TABLE 1

Showing results obtained by the injection of calcium chloride in cases of intestinal tuberculosis

NUMBER	DIAGNOSIS	LUNG CONDITION	DIARRHEA	PAIN	NUMBER OF INJECTIONS	EFFECT ON DIARRHEA	EFFECT ON PAIN	RESULTS
1	Tuberculous diarrhea	Very good	Yes	Yes	52	Markedly improved	Markedly lessened	Much better in every way; still under treatment
2	Tuberculous diarrhea	Very bad	Yes	Yes	2	0	0	Died
3	Tuberculous diarrhea	Bad	Yes	Yes	2	Slightly improved	Slightly lessened	Continues fairly well; no calcium chloride in past year
4	Tuberculous diarrhea	Bad	At times	General abdominal distress	5	Markedly improved	Markedly lessened	Went to Ohio; lost sight of
5	Tuberculous diarrhea	Very bad	Yes	Yes	2	0	0	Died
6	Tuberculous diarrhea	Very bad	Yes	Yes	2	0	0	Died
7	Tuberculous diarrhea	Bad	Yes	Yes	2	Slightly improved	Slightly lessened	Continued improvement; no bowel symptoms now
8	Tuberculous diarrhea	Very good	Yes	Yes	7	Markedly improved	Markedly lessened	Relapsed; operation; tuberculosis of small bowel found; died
9	Tuberculous diarrhea	Very bad	Yes	Not much	2	0	0	Died
10	Tuberculous diarrhea	Very bad	Yes	Not much	2	0	0	Died
11	Diarrhea, cause undetermined	Very good	Yes	No	1	0		In Chicago past six months; in fine condition
12	Tuberculous diarrhea	Very bad	Yes	Yes	1	0	0	Returned to Virginia in fair condition; lost sight of
13	Tuberculous diarrhea	Very bad	Yes	Yes	2	0	0	Died
14	Tuberculous diarrhea	Bad	Yes	No	2	Recovery		Bowels no longer cause trouble

15	Diarrhea, cause undetermined	Fair	Yes	No	1	0		In good condition; still has diarrhea at times
16	Tuberculous diarrhea	Bad	Yes	Yes	11	Moderately improved	Moderately lessened	Lung condition grew worse; went home; died
17	Tuberculous diarrhea	Very bad	Yes	Not much	3	0	0	Died
18	Tuberculous diarrhea	Good	Yes	No	15	Markedly improved		In good shape; lungs quite active; gone west to live
19	Tuberculous diarrhea	Very bad	Yes	Yes	2	0	0	Died
20	Tuberculous diarrhea	Very bad	Yes	Yes	3	0	0	Died
21	Tuberculous diarrhea	Very bad	Yes	Yes	2	0	0	Puerperal reactivation of old quiescent lesion; died
22	Tuberculous diarrhea	Very bad	Yes	Yes	2	0	0	Died
23	Tuberculous diarrhea	Fair but spreading	Yes	No	2	0	0	Died
24	Tuberculous diarrhea	Bad	Yes	Yes	2	0	0	Lost sight of
25	Tuberculous diarrhea	Good	Yes	No	5	Markedly improved	Markedly lessened	Doing finely; still under treatment
26	Tuberculous diarrhea	Fair	Yes	Not much	6	Markedly improved	Markedly lessened	Doing finely; still under treatment
27	Tuberculous diarrhea	Very bad	Yes	Yes	2	0	0	Died
28	Tuberculous diarrhea	Fair	Yes	Yes	4	Slightly improved	Slightly lessened	Going downhill; still under treatment
29	Tuberculous diarrhea	Very bad	Yes	Yes	4	0	0	Died
30	Tuberculous diarrhea	Very bad	Yes	Yes	2	0	0	Dying

and three received one injection (11, 12, 15). The three cases receiving one injection each included the two mentioned above in which a diagnosis of tuberculous diarrhea was very questionable, and the third case was *in extremis*.

Of the sixteen cases receiving two injections each, thirteen (2, 5, 6, 9, 10, 13, 19, 21, 22, 23, 24, 27, 30) showed absolutely no beneficial effects therefrom and the drug was consequently discontinued. Two of the patients receiving two injections each (3, 7) showed decided improvement, which has continued and consequently no further injections have been given. One patient (14), receiving two injections at an interval of two months, was relieved of all symptoms and has not needed another dose.

The three cases receiving fifty-two, fifteen, and seven injections respectively (1, 18, and 8), deserve special emphasis for two reasons. In the first place they were under observation for a longer period of time than the others, and in the second place in two of them (1 and 8) pulmonary involvement was so slight as to play a negligible rôle, while the intestinal symptoms were the dominant factor. In one case (1) bowel movements were reduced in number from five to one or two daily. Furthermore, prior to the administration of calcium chloride, a moderate amount of codeine had been necessary to reduce the movements to five daily and also to lessen the pain. Subsequent to the injection of calcium chloride, codeine was omitted and has since had to be taken only at rare intervals. The stools are also far better formed than formerly, and their odor is decidedly less offensive. Calcium chloride was started twenty months ago. At first, the effects of an injection of 5 cc. lasted apparently a month. After the first three months, however, the bowel movements increased in frequency at the end of three weeks. It is now necessary to give calcium chloride every ten days in order to maintain a satisfactory intestinal condition, and the amount injected has been increased from 5 to 8 cc. The question arises whether the interval will have to be still further shortened and the dose still further increased, and whether in the end the beneficial effects of this drug will be lost. Time alone can tell. This patient has had the only severe reaction to calcium chloride that we have seen. It occurred some three months ago and consisted of a chill, coming on about four hours after the injection of 9 cc., fever to 102°F., severe abdominal pains and a profuse watery diarrhea. These symptoms passed off in forty-eight hours, and although many injections have been given since, they have never recurred.

The case having seven injections (8) is also most instructive. This patient came to us with slight, old, bilateral, quiescent, apical lesions, but having from three to five watery and foul stools daily, and suffering much abdominal pain. At the time of his arrival he was taking two grains of codeine daily by mouth to control both diarrhea and pain. Calcium chloride on the first injection wholly eliminated the pain, which never returned, and restricted the stools to from two to three daily, without the use of any codeine whatsoever. Injections were repeated at first every three weeks, later every two weeks. Despite the improvement in symptoms and in general comfort, this patient lost weight very slowly but uninterruptedly. Radiographs showed a decided hypermotility in the cecum and ascending colon. The patient was referred to Dr. Brown of Saranac Lake, and to Dr. Archibald of Montreal, who has had the largest experience of anyone in the operative treatment of these cases, and, our diagnosis being corroborated, the abdomen was opened with the intention of doing a resection of the involved area. At operation, however, there was found, in addition to colonic tuberculosis, an extensive involvement of the small intestine, this rendering the case inoperable so far as eradication of the disease was concerned. Subsequently, the patient lost steadily and finally died.

The patient receiving fifteen injections (18) presented rather marked pulmonary signs, but was not acutely ill. From the start, in August, 1920, calcium chloride acted very well, reducing bowel movements and controlling pain. He has taken his injections, never over 6 cc., at intervals of about a month. His bowel condition is excellent and he went to New Mexico a few days ago in the hope that that climate would benefit his pulmonary condition, which has remained stationary.

One of the cases receiving five injections (4) has suffered, in addition to the symptoms due to a very extensive but not too active unilateral lung involvement, from repeated, so to speak, "explosive," attacks of diarrhea accompanied and followed by abdominal distress, hardly amounting to actual suffering but none the less very disturbing to the patient. Calcium chloride aided greatly in lessening diarrheal attacks, and also almost completely dispelled abdominal pain. Injections were given every two weeks: The patient left Asheville and returned to his home in Ohio, where we hear he is holding his own. We do not know whether the administration of calcium chloride has been continued.

The other case receiving five injections (25) has done and is doing exceedingly well. Bowel movements have been reduced and pain has been abolished. Appetite and digestion have greatly improved. This case is using the Alpine lamp and is also being treated with artificial pneumothorax. From a desperately ill girl, she has been transformed into one whose outlook is distinctly bright.

We are daily learning more about the frequency and symptomatology of intestinal tuberculosis. The signs point to a time that will come as a result of more refined diagnostic methods and more radical and curative surgery, when intestinal tuberculosis will emerge from the position that laryngeal tuberculosis occupied twenty years ago (and from which it has now graduated) as one of the hopeless forms of tubercle. To-day, however, intestinal tuberculosis must be regarded as a very serious, though not altogether hopeless complication, and one that in the vast majority of instances presages a fatal outcome. The misery and distress of these patients is known to all of us. If we have at our command a remedy that will palliate, though it will not cure, we must use it.

The work of a number of men in recent years, beginning with Stierlin in Germany and crystallizing in the recent papers of Brown and Sampson in this country, gives us the hope of a discovery of a positive means of diagnosing tuberculous enteritis, though not as early a means as we could wish, and in a certain number of cases their work and that of Archibald would seem to indicate that surgery may yield a small number of cures. Meantime, we all of us are sadly put to it to find some theraupeutic measure that will help us to palliate if not to cure such a trouble. Hence the work of several Swedish physicians, showing that the intravenous injection of calcium chloride, would control the diarrhea and relieve the pain is gladly welcomed.

Our limited experience, and that of others, has convinced us that in calcium chloride we have a remedy, which will frequently palliate and relieve, and which, when we can diagnose our cases early, may even possibly prove curative. The results we have here presented are not brilliant, but, based though they are on a relatively small number of cases, their significance is such as to encourage us in the further use of the drug, feeling as we do that we have prolonged the lives of some, made others far more comfortable by the use of this method of treatment, and consequently that it should be given a fair trial by those who see enough of such cases to enable conclusions to be drawn as to its value.

At the same time it is to be hoped that the reason for its good effect can be worked out in our pharmacological laboratories, so that we can understand why we get results. Might we also suggest to those who have opportunity for investigation, that there are few problems in phthisiotherapy to-day more important than that of the early diagnosis and successful rational treatment of intestinal tuberculosis, and that he who is so fortunate as to make discoveries in this realm will be doing much to deprive of its terrors one of the most painful and distressing of human maladies.

STUDIES ON THE RESPIRATORY ORGANS IN HEALTH AND DISEASE

IV. A COMPARISON OF VITAL CAPACITY READINGS AND X-RAY FINDINGS IN PULMONARY TUBERCULOSIS[1]

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One of the very valuable aids we have to-day in the diagnosis of active pulmonary tuberculosis was called to the attention of the medical profession by John Hutchinson just three-quarters of a century ago. After inventing the spirometer Hutchinson (in 1846) took vital capacity readings on nearly two thousand men whom he later classified according to weight, height and age. He thus established a normal lung capacity for men of certain classes of given age and size. The chief object of Hutchinson's investigation, however, was to contribute a method of detecting disease. He therefore set to work to make a comparison of the vital capacity of healthy men with that of diseased men of the same size and age. In a series of cases of pulmonary tuberculosis (early stage) he found the mean vital capacity to be 2441 cc. instead of 3670 cc. in normal individuals of the same size and age. In another series (advanced stage) the mean vital capacity was 1360 cc. instead of 3605 cc. for normal men. Hutchinson's cases are so striking that it is impossible to refrain from quoting a few of them:

> A surgeon called upon me when in full practice; he looked in perfect health, and said he was so. I measured his vital capacity and found it to be 100 cubic inches below the healthy standard; four months afterward I heard he was ill, and that ausculation had given evidence of phthisis pulmonalis; a few months afterward he died of that complaint. This gentleman looked so remarkably well when I first examined him, that I was led to doubt the extent of reliance to be placed upon the spirometer, but the result entirely removed the doubt.
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> Another gentleman, holding an elevated position under Government, manifested great deficiency of vital capacity, and that too when performing his duties; but within four months his death took place, and extensive tubercular disease was found in the lungs.

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[1] Read in part before the Clinical Section at the Seventeenth Annual Meeting of the National Tuberculosis Association, New York City, June 16, 1921.

A young man of 11 stone, and 5 feet and 7 inches high, firm and muscular; his vital capacity was 47 cubic inches below the mark. Within one week of this time I had an opportunity of examining his lungs, and found the left lung at the apex studded with miliary tubercles, the whole not extending beyond a square inch, the entire remaining portion was to all appearances healthy.

In 1918 Garvin, Lundsgaard and Van Slyke reported the results of studies on 31 adult men suffering from pulmonary tuberculosis. In their 9 incipient cases the vital capacity was found to be diminished as a result of an increased residual air. In 22 moderately advanced cases "the vital capacity was substantially decreased, principally as a result of the diminished total capacity." In the same year these authors also reported the results of studies on 20 adult women suffering from pulmonary tuberculosis. Of the 8 women with incipient tuberculosis the vital capacity was somewhat decreased due to the increased residual air. In the 12 moderately advanced cases the vital capacity was materially decreased. Although only 51 cases were studied, this work was done and presented in an excellent manner.

The first report of another very thorough-going study of vital capacity in pulmonary tuberculosis was made in June, 1920, by Dreyer and Burrell. They reported the results of studies on 200 cases. In 116 of these cases the vital capacity was taken on more than one occasion. The conclusions of the authors are as follows:

1. In cases of pulmonary tuberculosis there is a definite decrease in vital capacity as compared with what should be normal for any individual, taking into account the class in which this individual should be placed according to occupation and mode of life.

2. An improvement in the clinical condition of the patient is found to be accompanied by an increased vital capacity, while an advance of the disease results in a decrease in vital capacity. The vital capacity, therefore, gives a valuable quantitative measure of the benefit, if any, which a patient receives as a result of treatment.

3. The determination of the vital capacity is useful for the classification of cases of pulmonary tuberculosis, because it is possible by this means numerically to express the injury to health (e.g., degree of toxemia) which otherwise would depend on the individual interpretation of physical signs by different observers. In this connection it should be noted that classification by physical signs alone may place a patient nearing death from an acute lesion in a high category, while another patient, with satisfactory fibrosis and extensive cavitation, likely to live for several years, may be placed in the lowest category.

4. As an aid to diagnosis a single or repeated examination of the vital capacity of doubtful cases will also prove useful. If a normal vital capacity is found in such cases, the patient is most unlikely to be suffering from pulmonary tuberculosis, whereas, if the vital capacity is much decreased the patient should be suspect, though it must always be borne in mind that other diseases may also cause a lowering of the vital capacity.

5. Finally, a systematic study of the vital capacity in its proper relationship to body size has given important information as to the beneficial effects of different treatments of pulmonary tuberculosis, and has made it possible to distinguish quantitatively the degrees of improvement.

Wittich, Myers and Jennings (1920) reported the results of observations on 82 tuberculous patients. This series includes both women and men. The 20 cases with stage I disease showed a vital capacity considerably below the normal. The vital capacity was markedly decreased in the stage II and III cases. In 24 cases a second series of readings was taken, three to six months after the first readings and the results were as follows:

Of the 9 cases whose physical signs caused them to be reported in worse condition, eight showed all three constants indicating progressive disease, while readings for the ninth would suggest stationary or slight improvement. Of the eight cases whose clinical reports were disease stationary, the vital capacity blown in every instance indicated a slightly worse condition. Of the seven cases whose reports were condition improved, the measures of only two confirmed such report, and five showed constants pointing toward a stationary or slightly progressive disease.

OBSERVATIONS

This study includes a series of 101 cases (48 male and 53 female), some of which appeared for examination because of certain symptoms, definite exposure or previous diagnosis of pulmonary tuberculosis, while others had recently been diagnosed as cases of frank pulmonary tuberculosis and were referred for sanatorium treatment. In each case a careful history was taken and a physical examination of the lungs was made.

The actual weights of the individuals are net, while the given height is without shoes. For ascertaining the normal (theoretical) weight the *Tables of Standard Weight According to Height and Age* of the Prudential Insurance Company of America were used. Inasmuch as the weights in these tables are not net the weight of clothing was deducted according to the method of Quetelet mentioned by Hutchinson (1846). The trunk length was taken in the manner described by Dreyer (1919), and Dreyer's tables (1921) were also used in ascertaining the theoretical normal weight of the patients. The graphic chart of DuBois and DuBois was used exclusively in obtaining surface area.

The lung capacity was taken with the water spirometer made according to the specifications of Peabody and Wentworth (1917). Each patient was first instructed as to the use of this instrument, then given at least three trials and the highest reading was recorded.

Before Dreyer's tables were available the writer made a table in which the normal vital capacities for women were calculated according to Dreyer's formula, $\frac{Wt:^{72}}{V.C.} = K$. The value of K was ascertained from actual observations on 138 nurses, studied and reported by West (1920) and Myers (1921). This value was found to be approximately 0.85. In the present study the normal vital capacities for women were taken from this table and used in the calculations of the lung capacity percentages. In the case of men the normal weight was ascertained from the table of the Prudential Life Insurance Company and the normal vital capacity was calculted from Dreyer's formula, $\frac{Wt:^{72}}{0.69}$ = vital capacity.

Dreyer and Burrell (1920) pointed out "that with loss of weight a vital capacity definitely abnormal, when calculated in relation to the normal weight of the person, might appear normal if calculated in relation to the reduced weight during disease." Inasmuch as many tuberculous patients are more or less emaciated while a few are overweight, particularly during or after sanatorium treatment, the trunk length was taken in most cases; and Dreyer's tables (1921) were used in ascertaining the normal vital capacities calculated according to the trunk length.

The physical fitness percentage was calculated first from Dreyer's surface area formula (the normal weight being taken from the Prudential Life Insurance Table) and second from Dreyer's stem length formula. The amount of air exhaled per square meter of body surface was also computed. The actual weight of the patient was used in making this calculation. In each case, therefore, the physical fitness percentage was calculated according to the above three methods. The average of the three is presented in table 1 as the physical fitness of each individual.

Frequent fluoroscopic examinations were made, in order to obtain such information as the excursion of the diaphragm; but in the diagnosis of early disease no dependence whatever was placed on this instrument. Stereoscopic X-ray plates were made in all cases (with one exception in which a single plate was made) and in order to secure uniformity nearly all the plates were made by the same roentgenologist.[2]

The patients were grouped as (1) *suspected cases*, in which lung capacity readings and X-ray findings were approximately normal, (2) *cases of peribronchial tuberculosis* and (3) cases of *parenchymatous tuberculosis*. The second and third groups were again divided into unilateral and bilateral cases, and arranged in the order of extent of lesions revealed by the stereoscopic plates.

The first group includes 12 patients (6 women and 6 men) who came in for examination because of definite exposure, rapid loss of weight and strength, slightly streaked sputum or a previous diagnosis of active pulmonary tuberculosis. In most of these cases the vital capacity was found to be within normal limits. In order to confirm these findings, however, stereoscopic plates of the chest were made. In each case such plates showed no evidence of pathological changes.

Case St. 4 showed a lung capacity which was approximately 17 per cent below the normal. This patient has been under observation for several months and nothing has been discovered to account for her reduced capacity, except that she is 15 per cent overweight. Obesity is a factor, which as Hutchinson pointed out, tends to reduce lung capacity. Case St. 8 has a lung capacity reduced 15 per cent below the normal. While such a reduction closely approaches the border line between the normal and the diseased individual, the X-ray plates and physical findings revealed nothing to account for the decrease in this case.

In the small series of 12 cases, one patient was given a diagnosis of active pulmonary tuberculosis a few months ago while three other patients were not only given a diagnosis of active pulmonary tuberculosis, but were reported and sent to a sanatorium.

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[2] I desire to express my thanks to Doctors R. G. Allison and R. E. Morse for their aid and coöperation in the interpretation of the stereoscopic plates.

There are 20 patients in the second group (10 men and 10 women) who came in because of one or more of the following reasons: slight cough or expectoration, a generally run down condition, occasional chest pain, slight hemoptysis, or frequent "colds on the chest." The vital capacity in these cases was found to be normal or slightly below. Nevertheless, stereoscopic plates revealed unilateral or bilateral peribronchial infiltration.

Stereoscopic plates of the 10 women showed peribronchial tuberculosis on one side in 7 cases and on both sides in 3 cases. In some cases this was small while in others it was large in amount.

The lung capacity in this series of women ranged from 82 per cent to 104 per cent of the (theoretical) normal. There was only one patient as low as 82 per cent.

In the series of 10 men, stereoscopic plates showed all but one to have unilateral peribronchial tuberculosis. The lung capacity of the entire series ranged from 76 to 112 per cent of the (theoretical) normal. The patient (T. 12) whose lung capacity was 81 per cent of the normal is a Filipino who gave a history of having had a chronic disease (not tuberculosis) in childhood which evidently interfered later with his nutrition and development. This patient now weighs 88 pounds which he asserts is as much as he ever weighed. Physical examination of this man's chest revealed no evidence of active pulmonary tuberculosis, while the stereoscopic plates showed only a slight peribronchial infiltration in the left upper lobe.

In case T. 11 (a Hindu medical student) the stereoscopic plates showed a slight peribronchial tuberculosis in the left apex with marked emphysema in the base of each lung. The lung capacity was found to be 76 per cent of the normal. The emphysema undoubtedly contributes largely to the decrease in lung capacity in this case.

Case T.13 had a lung capacity 18 per cent below the normal. The physical examination was negative and the stereoscopic plates showed only a slight peribronchial infiltration in the first interspace. Nevertheless this patient was in a marked state of debility and two weeks later developed a psoas abscess.

In the cases of mild peribronchial tuberculosis, many were permitted to continue their activities with the understanding that they lead a well regulated life. Frequent subsequent lung capacity readings have been found of great aid in ascertaining the patients' ability to work in spite of the disease. The question sometimes arises as to whether every patient whose X-ray plates reveal tuberculosis of the peribronchial type should be sent to a sanatorium. Of course this is at present a physical impossibility because of the limited capacity of our sanatoria. Is there any more reason, however, why these patients who show and maintain a physical fitness well within normal limits under work should be sent to a sanatorium than that every person without symptoms who gives a positive tuberculin test should be? In this small series of cases, patients have been found in the sanatorium who give no history of having any cardinal symptoms of tuberculosis, and the physical fitness is approximately 100 per cent, yet the X-ray plates show slight evidence of peribronchial tuberculosis. Such procedure is unfair to thousands of patients with active tuberculosis who really need sanatorium care.

There are 69 cases (37 female and 32 male) in the third group. Most of the cases in this group came in with one or more of the cardinal symptoms of pulmonary tuberculosis, while physical examination revealed evidence of disease. The majority of the moderately advanced and far advanced cases showed a reduction in lung capacity, which corresponded reasonably closely with the extent of the lesion interpreted from the stereoscopic plates. However, in a few cases the plates revealed evidence of extensive bilateral tuberculosis with cavitation, while the lung capacity was within 70 per cent or more of the normal. In a few other cases the lesions appeared very small while the lung capacity was much reduced.

Of the 37 women in this group, the stereoscopic plates revealed parenchymatous tuberculosis only on one side in 20 cases. The amount of disease ranged from a very small area to that which involved a whole lung; and in one case the diseased lung was completely collapsed by artificial pneumothorax.

The lung capacity in this series ranged between 42 and 103 per cent of the normal. Stereoscopic plates of the patient whose lung capacity was reduced to 42 per cent revealed tuberculosis with cavity formation on the left side to the fourth rib. The right lung showed some peribronchial thickening in the upper lobe, but was free from parenchymatous involvement. In the patient whose lung capacity was 103 per cent, the stereoscopic plates revealed tuberculosis in the first and second interspaces on the right side. However, this patient had been in the sanatorium three months, when her lung capacity was taken.

Another case, almost identical with the last one so far as X-ray plates are concerned, had a lung capacity reduced to 61 per cent of the normal.

Stereoscopic plates of the remaining 17 women in the third group showed evidence of bilateral parenchymatous tuberculosis. The extent of the disease ranged from a very slight lesion on each side to disease which involved the greater part of both lungs.

The lung capacity in this group ranged between 26 and 108 per cent of the normal.

Of the 32 men with parenchymatous tuberculosis the stereoscopic plates showed unilateral disease in 11. The lung capacity ranged from 81 to 119 per cent of the normal. The patient with 119 per cent developed active tuberculosis early in 1918, and was sent to a sanatorium for treatment. After nearly a year of treatment this patient returned to work and has suffered no relapse. Although his lung capacity is very good the stereoscopic plates still show definite tuberculosis in the extreme apex of the right lung. In the remaining 21 men the X-ray plates show parenchymatous tuberculosis on both sides. The lung capacity ranged from 36 to 115 per cent.

In this study, it was very fortunate that, in a few persons who were or had been students in the University of Minnesota, lung capacity records taken when they were college freshmen were still available in the department of physical education.

For example, case T. 67 showed a lung capacity of 4400 cc. while his theoretical capacity was only 4453 cc. Apparently there was no impairment; but the patient gave a history of previously having taken a considerable part in athletics; therefore, the question arose as to whether the patient had not overdeveloped his lung capacity. On examining his record taken by Professor L. J. Cook two years before, it was found that he had a lung capacity of 4978 cc. Therefore, this patient's actual lung capacity was reduced and the X-ray examination revealed evidence of very definite parenchymatous involvement in the left upper lobe.

Another similar case is that of a young lady (T. 41) who came in with cardinal symptoms of active pulmonary tuberculosis and showed physical signs of minimal disease. Her actual lung capacity was 2400 cc. while her normal (theoretical) capacity was 2966 cc. From Doctor Anna Norris's office in the Department of Physical Education it was found that this patient had a lung capacity of 2800 cc. in April, 1920. Inasmuch as the stereoscopic plates revealed evidence of early tuberculosis in both lungs, one could feel reasonably sure that this is the cause for the recent decrease in lung capacity.

In another patient (T.75) the lung capacity was found to be approximately the same as his theoretical capacity, yet X-ray plates showed definite parenchymatous tuberculosis in both upper lobes. The records in the department of physical education showed that eight months previously his capacity was nearly 400 cc. below the present capacity. It would appear, therefore, that his condition may have improved considerably during the last eight months. Further observation, however, may throw more light on this case.

In many of the sanatorium cases a second reading has been taken since the diagnosis was recorded. These subsequent readings are very valuable in that they throw much light on the manner in which the patients are responding to treatment. In one case the first examination showed a lung capacity of 2550 cc., while the second reading taken after three months of postural rest in a sanatorium revealed a decrease of 350 cc. On the other hand, case T. 29 had a lung capacity of 1900 cc. on first examination, but after three months of sanatorium treatment her capacity had increased 900 cc. Other similar observations lead one to conclude that the lung capacity test is at least as valuable as X-ray examination in following the results of treatment. Moreoever, spirometer readings are more easily and much more cheaply obtained.

There is no small individual variation in vital capacity. It depends upon many factors, such as physical development, occupation, nationality and age. Therefore, lung capacity readings in any given case are of greater significance when the individual's normal has previously been established by actual observations, at a time when that individual was in good health. Any subsequent deviation of more than 15 per cent from that normal is significant. It is only when this deviation is below the normal, however, that it becomes of clinical significance.

Our present methods of calculating a person's normal capacity are based on averages taken from actual observations on a number of individuals, from surface area formulae, etc. While these methods are reasonably accurate, they cannot be applicable in every case. In the case of T. 78, the patient was found to be definitely tuberculous, yet his lung capacity was 115 per cent of the normal. Inasmuch as this patient had previously played a wind instrument quite extensively over a period of a few years, we infer that his usual lung capacity is much beyond that observed. On the other hand, case T. 12 showed a lung capacity decreased to 81 per cent, yet the complete examination revealed nothing more than a slight peribronchial infiltration in the left lower lobe.

Inasmuch as this patient is a native of the Philippine Islands, and claims to have had a chronic disease in childhood which materially interfered with his subsequent nutrition and development, we infer that this individual has never had a lung capacity as high as his theoretical normal. In the last two cases cited our inferences may be correct, but we have no way of proving them.

In many colleges and universities, as well as in the public schools of some of our great cities, the lung capacity becomes a part of the permanent record of each enrolled student. This is indeed a very laudable procedure and deserves to be more generally adopted. Industrial organizations will find it well worth while to record the lung capacity of every employee on admission. In such cases disease may be detected which might otherwise remain undiscovered. Subsequent readings will be found of great value in the detection of early disease, or in ruling out disease of clinical significance which an individual may claim to have contracted as an employee.

CONCLUSIONS

To draw any sweeping or final conclusions from observations on such a small number of cases is indeed hazardous. However, the following conclusions appear to be justified:

1. In cases suspected of having pulmonary tuberculosis the lung capacity test is very valuable in diagnosis. If there is a reduction of more than 15 per cent, it is usually of clinical significance: however, other pulmonary and cardiac diseases may cause such a decrease. In view of these facts the spirometer is not sufficient in itself, but stereoscopic plates are usually necessary, and in many cases further tests and examinations must be employed.

2. There is considerable individual variation in normal lung capacity on account of such factors as occupation, mode of living, past physical training and development. Therefore, spirometer readings are most valuable in a person whose normal capacity has been established by actual observation at some time when that person was in good health. Otherwise, the reading might appear normal or even above, and still be reduced several hundred cubic centimetres. In all questionable cases X-ray plates are indispensable.

3. In cases of peribronchial tuberculosis, X-ray plates are usually necessary in diagnosis, since in many such cases the lung capacity is well within normal limits.

4. In parenchymatous tuberculosis the lung capacity test is valuable in ascertaining the severity of the lesion when other factors are excluded. It is not so valuable in determining the extent of the disease, for a very small severe lesion may reduce the lung capacity in one case more than occurs with a low grade extensive lesion in another case. Therefore, X-ray plates are more valuable in outlining the extent of the disease.

5. In some cases of fairly extensive fibrous and calcified tuberculosis the lung capacity is within normal limits. However, in most cases it is sufficiently reduced to indicate impairment of function if the disease is of clinical significance.

6. The most valuable service of the spirometer is in following the course of disease after the diagnosis has been made. This instrument registers an increase in capacity from time to time, as the disease comes under control. On the other hand, a decrease is registered in those cases that become progressively worse. For this particular work the spirometer is of more service than the X-ray; and the readings are more easily and more cheaply obtained.

7. The spirometer measures the ability and power of the lungs to function, while the X-ray records the nature and extent of the disease. Therefore, each has a different part to play. Neither one is infallible, but both are very valuable.

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TABLE 1

Classified results of observations

NUMBER	SEX	AGE	PHYSICAL FITNESS
Suspected cases			
			per cent
St. 1	Female	21	99
St. 2	Female	28	113
St. 3	Female	22	91
St. 4	Female	40	82
St. 5	Female	28	94
St. 5a	Female	33	90
St. 6	Male	19	104
St. 7	Male	20	118
St. 8	Male	19	85
St. 9	Male	25	101
St. 10	Male	27	122
St. 11	Male	48	101
Peribronchial tuberculosis Unilateral			
T. 1	Female	16	82
T. 2	Female	21	104
T. 3	Female	23	101
T. 4	Female	31	106
T. 5	Female	20	99
T. 6	Female	21	94
T. 7	Female	18	95
Bilateral			
T. 8	Female	20	101
T. 9	Female	21	87
T. 10	Female	24	102
Unilateral			
T. 11	Male	20	76
T. 12	Male	31	81
T. 13	Male	33	82
T. 14	Male	33	101
T. 15	Male	25	112
T. 16	Male	22	93
T. 17	Male	20	89
T. 18	Male	24	82
T. 19	Male	22	85

TABLE 1—*Continued*

NUMBER	SEX	AGE	PHYSICAL FITNESS
Bilateral			
			per cent
T. 20	Male	25	110
Parenchymatous tuberculosis Unilateral			
T. 21	Female	20	100
T. 22	Female	19	74
T. 23	Female	29	80
T. 24	Female	38	102
T. 25	Female	33	82
T. 26	Female	14	73
T. 27	Female	17	85
T. 28	Female	22	67
T. 29	Female	29	64
T. 30	Female	18	103
T. 31	Female	21	88
T. 32	Female	40	85
T. 33	Female	20	79
T. 34	Female	22	42
T. 35	Female	28	86
T. 36	Female	21	86
T. 37	Female	26	75
T. 38	Female	24	79
T. 39	Female	27	71
T. 40	Female	24	48
Bilateral			
T. 41	Female	20	80
T. 42	Female	30	90
T. 43	Female	33	108
T. 44	Female	25	78
T. 45	Female	14	52
T. 46	Female	26	64
T. 47	Female	21	81
T. 48	Female	30	86
T. 49	Female	25	43
T. 50	Female	29	54
T. 51	Female	24	58
T. 52	Female	25	63
T. 53	Female	20	67

TABLE 1—*Concluded*

NUMBER	SEX	AGE	PHYSICAL FITNESS
Bilateral—*Concluded*			
			per cent
T. 54	Female	45	61
T. 55	Female	25	65
T. 56	Female	51	60
T 57	Female	37	26
Unilateral			
T. 58	Male	27	81
T. 59	Male	28	96
T. 60	Male	30	119
T. 61	Male	24	94
T. 62	Male	23	78
T. 63	Male	24	88
T. 64	Male	38	89
T. 65	Male	22	92
T. 66	Male	35	88
T. 67	Male	22	99
T. 68	Male	25	98
Bilateral			
T. 69	Male	29	53
T. 70	Male	23	98
T. 71	Male	40	93
T. 72	Male	35	82
T. 73	Male	22	81
T. 74	Male	22	84
T 75	Male	18	101
T. 76	Male	45	80
T. 77	Male	26	88
T. 78	Male	21	115
T. 79	Male	24	60
T 80	Male	21	83
T. 81	Male	38	36
T 82	Male	22	46
T 83	Male	38	69
T 84	Male	58	78
T. 85	Male	36	50
T 86	Male	42	59
T 87	Male	26	49
T. 88	Male	27	50
T 89	Male	17	39

THE GRIFFITH METHOD FOR THE DIRECT ISOLATION OF TUBERCLE BACILLI

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Uncertainty of successful results in the majority of methods proposed for direct isolation of tubercle bacilli from sputum and other fluids or excreta has led to a general feeling that the most reliable procedure is to resort to inoculation of animals, with subsequent isolation from the tissues at autopsy. Objections to this procedure are that possible changes in virulence or growth characteristics may occur in the organisms as a result of animal passage and, also, the length of time required before final isolation in pure culture. In the usual direct methods the manipulations involved favor the chance of contaminations. A method which was at the same time simple and uniformly successful would be welcome. That proposed by Petroff (1) constituted a step forward, but did not greatly reduce the manipulations necessary and, without the use of gentian violet medium, did not yield as high a percentage of non-contaminated tubes as could be desired.

In 1914 and again in 1916, Griffith (2) (3), in articles dealing with types of tubercle bacilli found in sputum, made brief note of a method which he was using for the direct cultivation of his strains. The simplicity and reliability of the method, and the fact that it did not seem to have become generally known, made it appear to warrant further investigation. As described by him, equal parts of sputum and 10 per cent antiformin were mixed by shaking or stirring in a test tube, and a loopful of the mixture, after it has become partly liquefied, streaked directly onto suitable media. There was thus no sedimentation or washing, which is ordinarily thought necessary to overcome the inhibitory effect of the antiformin. In this way Griffith obtained cultures from 26 out of 31 specimens.

In the present investigation, essentially the same technique was used. Although previous work had shown that successful results could be obtained when the final concentration of antiformin was as low as 2.5 per cent, the greater number of contaminated tubes made it seem advisable to use the higher strength.

Sputum, preferably the early morning specimen, used for culturing, was collected in a sterile petri dish, but no further precautions, such as washing the specimen, were taken. Equal parts of sputum and 10 per cent antiformin by volume are mixed in a stoppered agglutination tube. About 2 cc. is a convenient amount. This is measured by rough graduations on the tube, rather than by attempting accurate measurement with a pipette. The mixture is well shaken and cultures made at the end of five minute intervals from five to thirty minutes.

The following media were used at different times during the work: (1) plain egg, original Dorset formula, (2) 1 and 5 per cent glycerin egg, (3) liver-egg (four parts egg to one of fresh calf's liver infusion), (4) liver-egg with 5 per cent glycerin, (5) egg medium with 1 per cent inulin, and (6) egg medium prepared according to Petroff's formula but without gentian violet. No dye was incorporated in any of the media, because, it was desired primarily to test the reliability of the technique, as judged by the number of uncontaminated pure cultures obtainable.

The liver infusion is prepared in essentially the same manner as ordinary beef infusion. Five hundred grams of finely chopped fresh liver (calf or beef) are soaked over night in the cold with 1000 cc. of tap water. The next morning the infusion is brought slowly to the boiling point, boiled for five minutes, and then filtered through paper. The use of liver suggested itself from the author's favorable experience with the ordinary liver agar (Dopter) for the cultivation of meningococci and gonococci. At that time it was found that the usual stock strains of tubercle bacilli grew luxuriantly on such a medium. It was hoped that with a large series of cases cultured at the several intervals, some one interval could be shown to be the most favorable for routine procedure, and thus still further simplify the method. Unfortunately, this did not prove wholly true. The several media were used for comparison with the liver medium, which constituted a slight modification of the various media at present generally used for the cultivation of the tubercle bacillus.

A total of 56 separate cases was cultured. The number of tubercle bacilli in stained smears of sputum used for cultures varied from those containing innumerable organisms to the microscopic field to sputum in which no acid-fast organisms could be found on the slide examined. The majority of specimens showed from one to ten bacilli to the field. Ten cases with only a Gaffky I count were cultured and there were two cases in which no bacilli were found on microscopic examination. These negative specimens had, however, been positive at some time during the patient's stay at the hospital. As mentioned above, no special precautions were taken to obtain a perfectly clean specimen and many were not as good as could be desired, often containing much saliva and many secondary microörganisms.

Tubercle bacilli were isolated in pure culture from all but one of the cases. It was usual to have good uniform growth on tubes of some media at all intervals, without growth of secondary forms. Over 90 per cent of the specimens yielded pure cultures without contaminations in any of the tubes. Out of a total of 1080 tubes throughout the whole study, only 50, or 4.5 per cent, showed any contaminations. As a rule such contaminations, when they did occur, consisted of one or two single colonies, and the tubercle bacillus colonies could easily be fished in pure culture. Contaminations were usually confined to tubes seeded at the five minute interval, and not always in all of these tubes. In only five cases did secondary growths run beyond this point. In one case 13 tubes out of 25 were contaminated, the next highest being 7 out of 25. It was rare to find over one or two contaminated tubes in the series, and almost never beyond the five minute interval.

Usually, as stated above, good growth was obtained at all intervals on suitable media. Although generally true, this did not hold for all specimens examined, so that the hope that one single definite time interval could be selected as most suitable and applicable to all specimens was not fulfilled. Except for a small number of specimens, the ten minute interval could be taken to yield pure cultures without contaminations. Some few, however, showed distinct variation, in that growth might occur at only one or more of the several intervals without appearing on the tubes seeded before or after. It was often true, where growth occurred throughout the series, that the most luxuriant growths were obtained on the twenty to thirty minute transplants. Undoubtedly, as Griffith suggested, several factors enter into such variations, such as the character of the original specimen and the readiness with which it digests, the possibility of some of the organisms which appear on the stained smear being dead, and undoubtedly an individual susceptibility of strains to the action of antiformin. One case in the present series, a strongly positive sputum, was cultured five times with only one positive result after the first trial, in which growth occurred only on three out of five tubes at the five minute interval. Again, in another case, growth was obtained in only three of the five minute tubes, and these tubes showed, respectively, heavy seeding in the first, 6 colonies in the second and 3 in the third tube, exactly in the order in which they were planted, an interval which was never more than thirty seconds. Only one example of the other extreme was noted. In this case growth appeared only on the tubes seeded after thirty minutes. This would appear to indicate that different strains show marked variation in their ability to withstand the action of antiformin.

The first appearance of growth (visible to the naked eye) varied from six days at the earliest up to thirty days in one case. Twenty-eight per cent of the specimens showed growth in ten days or less, and 73 per cent before the fifteenth day. Here again this was not dependent upon the number of tubercle bacilli present in the stained sputum. Of the several kinds of media used the most uniformly successful from the several viewpoints, that is, earliness of initial appearance of growth, heaviness of seeding and final luxuriance of growth, was that containing liver infusion, either with or without glycerin. This medium was always far superior to the Dorset medium, and, in the majority of cases, surpassed all other media. A rather interesting point was that almost invariably the liver-egg (without glycerin) showed initial growth well before any of the other media, although eventually (at five weeks, when the final reading was made) media containing glycerin, in particular the glycerin liver-egg, might show a greater final luxuriance.

CONCLUSIONS

In 55 out of 56 specimens tubercle bacilli were isolated in pure culture by the Griffith direct method.

Less than five per cent of a large number of tubes showed any contaminations.

The most uniformly successful medium for the direct isolation of tubercle bacilli from sputum was one containing beef liver infusion in the proportion of one part infusion to four parts of egg.

The simplicity and uniformly successful results with this method constitute a distinct advance over other methods at present in use for the direct isolation of tubercle bacilli from sputum.

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THE DISSEMINATION OF BACTERIA IN THE UPPER AIR PASSAGES

I. THE CIRCULATION OF FOREIGN PARTICLES IN THE MOUTH

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As the study of the mechanism of respiratory infection has progressed, it has become evident that the process is much more complicated than previously had been supposed. Until recent years it was thought that the mouth could be regarded as a large culture tube, containing a medium favorable for a great number of microörganisms, and that any chance bacterium which gained entry might colonize and bide its time until by some "lowering of resistance" of the host it was enabled to penetrate the tissues and set up disease.

Recent studies, however, on the fate of bacteria introduced into the upper air passages (1) have shown the facts to be quite the opposite, namely, that the normal mouth offers a very poor soil for the growth of foreign bacteria, and that a very effective mechanism exists for disposing of them. In other words, special combinations of circumstances of a fortuitous nature (for the microörganism) are necessary before colonization, invasion, and carrier states can occur. Furthermore, it has been pointed out that some types of germs seem to grow free on the mucous surfaces, whereas others are localized in a focus of diseased tissue (2); and it was suggested that such distinctions cannot be explained by any known criteria of test tube growth, but that for the time being we must assume inherent or acquired variations in adaptation (3), begging the question of the ultimate explanation.

It has seemed to us that information about the more intimate relations of these various types of bacteria to the mucous membrane might result in an advance in the solution of the general problem. The question can perhaps be most clearly stated by sketching the hypothetical fate of a foreign microörganism deposited in the mouth. One may conceive of it, first, as resting on the layer of mucus which everywhere covers the epithelial surfaces. A variety of possibilities immediately come to mind as to its subsequent fate. It may fail to penetrate the mucus and may be washed away and eliminated, or it may reach the epithelium and establish some form of growth in relation to the tissue surface. It may set up a reaction in some anatomically isolated spot, such as the tonsil crypts, it may be removed by phagocytosis, or, finally, it may be able to colonize with the production of an acute inflammation.

In an attempt to analyze the factors involved, simultaneous cultures were made from various sites in the same individual—pharynx, nose, tongue, and tonsils (4). It was found that the benign, habitual mouth flora is more or less uniformly distributed throughout the buccal cavity, but that foreign microörganisms, when persistently present, were confined to a localized region. This fact in itself was not remarkable, inasmuch as the bacteria were probably associated with a focus of infection; but we were surprised to find that there was little or no apparent spread from such a focus to the general mouth cavity. Repeated cultures, for example, from a person who harbored Staphylococcus aureus, yielded the bacteria in large numbers from both tonsils, but not from the tongue or pharynx. Such observations as these suggested, first, that the circulation of microörganisms in the mouth might be modified by the overlying layer of mucus, and secondly, that there might be definite currents in these regions which regulated the distribution of foreign bacteria. Were this so, it might be of great importance from the standpoint of infection in the individual, and also might throw light on the spread of bacteria to the outside world with the consequent infection of others.

The present work, therefore, deals with the circulation of fluids in the mouth, with studies on the paths of travel of bacteria after entering the mouth, with the relative ease with which they are discharged from various areas, and with the more intimate relations of bacteria to the mucous membranes.

THE CIRCULATION OF FLUIDS IN THE MOUTH

Before presenting the experimental facts, a few general considerations may be taken up. Reviewing briefly the various mucous membranes of the body, it is seen that each is supplied with an adequate system of drainage. Such a system consists of two elements, first, a discharge of mucous or serous secretion upon the membrane by intrinsic small glands and, second, some grosser mechanism for flushing the entire system. The bowel empties itself periodically and thereby prevents undue accumulation of noxious material; the urethra is kept practically sterile by the frequent passage of urine; the trachea, by its mucous secretion, by the sweep of its ciliated epithelium, and by cough rids itself with remarkable rapidity of inhaled foreign particles and bacteria; the conjunctiva is constantly washed by the lachyrmal flow which is quickly drained off by the lachrymal duct; the nose is kept clean by its current of ciliated epithelium and by its mucous secretion aided by the drainage from the lachrymal duct; and the mouth is constantly flushed by its intrinsic secretions from small mucous and serous glands plus those discharged into it from the salivary glands. Interference with drainage in any one of these areas promptly and invariably leads to serious disturbance of function,—intestinal obstruction, conjunctivitis, cystitis and other conditions may be mentioned.

Recognizing the general importance of the above principle, one would expect an especially adequate mechanism to prevail in such a region as the mouth which is constantly open to invasion by outside bacteria: it should be one which would remove foreign particles promptly and effectively, and preferably by a very direct route without spreading them over the entire surface. A mechanism of this sort would be especially important from the point of view of infection, should it turn out that the site of inoculation of the microörganism determines to some extent its course in journeying through the mouth cavity.

The following experiments were done in an attempt to determine the presence, if such exist, of regulated currents of flow in the mouth cavity.

ANATOMICAL CONSIDERATIONS

It will be recalled that the mouth in all its crevices and ramifications is lined by stratified squamous epithelium. This is characteristic of surfaces exposed to a certain amount of constant trauma, in distinction to the single layer of ciliated epithelium of more protected and delicate membranes, such as those of the deeper nasal passages and the trachea. Under normal conditions the buccal and pharyngeal surfaces are constantly moistened and lubricated by the serous and mucous secretions of innumerable, intrinsic, small glands. In addition there is the flow from the salivary glands—at times profuse but on the whole less constant and dependable.

The situation of the intrinsic glands may be summarized as follows (5):

Lips and cheeks (*mucous glands*):

Labial glands: a series of groups near the inner border of the lips.

Buccal glands: small scattered groups over cheeks.

Molar glands: well defined groups opposite molar teeth.

Gums: The gums are without glands.

Hard palate: A continuous layer of glands on either side of the oval white space.

Soft palate: Numerous glands opening on the inferior surface.

Tongue (serous and mucous glands):

Serous glands: surrounding circumvallate and foliate papillae.

Mucous glands: over posterior third of dorsum of tongue, behind serous glands.

Anterior mucous glands: two elongated groups meeting in front but diverging behind, opening on under surface of tongue.

Additional mucous glands: along edges.

Pharynx (mucous glands): Mucous glands, numerous in upper part.

It should also be recalled that the lips, cheeks, tongue, and pharynx consist essentially of powerful muscular masses, the contractions of which produce definite mechanical effects. During the constantly repeated act of swallowing, fluids are forced backward by these contractions. It is of special note that under these circumstances the pillars of the pharynx are drawn together in such a way that the tonsil is protected and sidetracked from the general current.

METHODS

The method employed consisted essentially of placing some colored substance, the dissemination of which could be actually observed at various sites in the mouth. Dyes were used at first, but they had the disadvantage of initial rapid diffusion, followed by prompt fixation in the tissues. Finally, powdered charcoal was selected as being quite satisfactory. The procedure used was as follows: A cotton swab was soaked in water and was then dipped into the charcoal. The moist powder was spread on the selected site over an area not greater than 1 cm. in diameter. After the application the person was instructed to act in a normal manner in regard to talking, laughing, and swallowing saliva, and was asked not to drink fluid until the experiment was concluded. The mouth was inspected at regular intervals, and attention paid to the following points: (1) the path of spread of the carbon particles (direct and by contact), (2) their rate of disappearance, and (3) the degree of adhesion at the site of application. Each experiment was repeated from five to ten times in various subjects. The results within slight limits dependent on anatomical and physiological variations agreed in every case.

EXPERIMENTS

Experiment 1. The fate of carbon particles placed on the tongue: The charcoal paste was first rubbed on the anterior, central part of the tongue over an area of about 1 cm. in diameter. Within the first thirty to sixty seconds there was no apparent change, except that some of the material was transferred by contact to the hard palate. After about one minute it could be seen that the carbon was travelling steadily backward in a band along the central part of the tongue (diagram 1). Within five to fifteen minutes the test substance had reached the line of the circumvallate papillae, but was still visible along its whole path from the site of application. At the circumvallate papillae and the lingual tonsillar tissue there was a partial and temporary arrest of the carbon which now gradually progressed in streaks through this area. Within thirty minutes to one hour (as a rule within the shorter period) no charcoal was anywhere visible in the mouth. *It is of special interest that there was never any spread forward on the tongue*, regardless of the position of the head or of the activities of the subject.

A similar experiment was next performed, with the carbon placed on the anterior dorsum of the tongue, to one side of the midline. Its fate was similar to that described above, except that the particles *never crossed the midline of the tongue* though they were frequently swept up to it (diagram 2).

Similar applications were next made on the posterior central and lateral aspects of the dorsum of the tongue. In these cases, depending on the anatomy of the particular subject, there was some transference by direct contact to adjacent areas, such as the anterior pillars, soft palate, and lower surface of tonsil (when very prominent). The time and manner of disappearance were similar to that described above and in no case was there any visible spread forward.

Comment on Experiment 1: From this experiment it appears that foreign particles adhere well to the dorsum of the tongue, as evidenced by lack of immediate spread to areas other than those in direct contact with the site of application. This result would be expected from the anatomy of the organ, with its papilliform surface and its overlying layer of mucus. Currents carry the particles directly backward without crossing the midline and without bringing them in contact with the tonsils or upper pharynx, except in occasional cases with markedly hypertrophied tonsils. The particles have usually disappeared within thirty to forty-five minutes. It is apparent, then, that an effective mechanism exists here for the rapid and direct removal of foreign particles, at the same time preventing a general spread throughout the mouth cavity. The protection of the tonsils is of special importance and will be further discussed below.

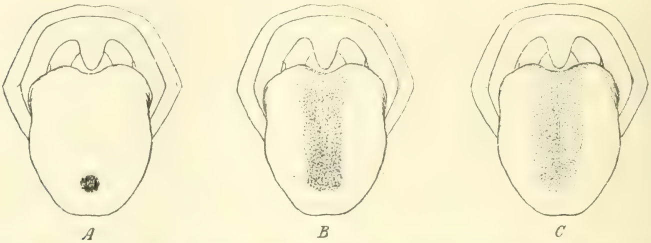

Diagram 1. Spread of Charcoal Particles Placed on the Anterior Central Portion of the Dorsum of the Tongue (Case H)

A. 10:39 a.m.: Appearance of tongue immediately after application

B. 10:44 a.m.: Rapid spread of carbon particles backward

C. 10:58 a.m.: Further spread along same path. Most of the carbon has disappeared from the original site of application.

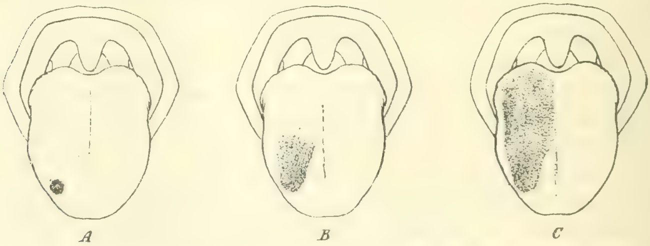

Diagram 2. Spread of Charcoal Particles Placed on the Anterior Lateral Portion of the Dorsum of the Tongue (Case C)

A. 10:42 a.m.: Appearance of tongue immediately after application

B. 10:48 a.m.

C. 11:04 a.m.: The particles have spread backward and up to, but not across, the midline.

The exact nature of the cause of these currents is a matter for speculation. Suction due to the contraction of the muscular masses of tongue, cheeks, and pharynx seems to be the most likely explanation.

Experiment 2. The fate of carbon particles placed on the palate: Application was first made on the anterior central part of the hard palate about 1 cm. from the gums. The carbon was promptly spread by contact over the entire anterior part of tongue. After one minute it was diffused over the entire hard palate in streaks and dots. Within five minutes the substance was practically gone from the palate, a few dots remaining in crevices in the mucous membrane. After ten minutes a few minute particles still remained as scattered dots. Within thirty minutes no carbon was any longer visible, save in one case, in which a single dot, adherent in a crevice in the mucous membrane, was still present after forty-five minutes. Application on the same part of the palate, but to one side of the midline, gave similar results, save that except for a few particles which crossed the midline the carbon remained almost entirely on the original side.

Charcoal, spread on the soft palate, was promptly transferred to adjacent parts of tongue. That remaining on the palate rapidly diffused in streaks and dots over the pillars and thence to the tongue. Within fifteen to thirty minutes it had disappeared from the site of application; except in occasional cases where a dot persisted in a crevice. *Spread was always backward and never forward.*

Comment on Experiment 2: Carbon particles placed on the palate adhered much less firmly than on the tongue. Since the former surface is much smoother, this was to be expected. The material seemed to be removed mainly by transferrence to the tongue, and disappeared from the site of inoculation usually in fifteen minutes. Anatomical variations, as in all of these experiments, play an important part, and lead occasionally to the abnormal retention of particles in crevices in the mucous membranes. On the whole, the mechanism of removal from the palate seems remarkably efficient. It is rapid and operates without contaminating the whole mouth cavity. It is of special note again that the currents are such as to avoid the tonsil.

Experiment 3. The fate of charcoal particles placed in the sublingual space: In this experiment some difficulty was encountered, owing to the smooth surface of the mucous membrane and the abundant flow of saliva from the submaxillary glands which was usually set up by the manipulation. As a rule, most of the carbon particles failed to adhere, but were carried rapidly back along the sublingual space and thus reached the posterior dorsum of tongue. In two subjects, whose salivary secretion was not free, it was possible to make the charcoal stick fast to the site of application. Within three to five minutes the material had practically disappeared, carried away by the mechanism described above, along the lateral sublingual spaces. After ten minutes a stippling of particles was still visible in crevices in the mucous membrane. Within twenty minutes the charcoal was all gone.

Comment on Experiment 3: Particles are promptly and rapidly removed from the sublingual space, especially as there is little tendency for them to adhere. Their removal is effected without general contamination of the mouth cavity, except in cases where an unusual abundance of saliva is present.

Experiment 4. The fate of particles of carbon placed on the buccal mucous membrane: Owing to the free flow of saliva from the parotid gland, conditions here were similar to those in sublingual inoculations. As a rule the saliva swept the test substance over the tongue and into the sublingual space, whence it was rapidly removed as described above.

Experiment 5. The fate of carbon particles placed on the posterior pharyngeal wall: Application of charcoal here was easy, as the latter adhered readily to the mucus on the corrugated pharyngeal surface. Within the first minute no change was apparent at the site of application. In some cases the dorsum of the tongue was stained by contact. After one minute a steady progress of the carbon particles down the posterior pharyngeal wall was apparent. When the application was made on one side, there was no spread beyond the midline. In no case did the particles come forward into the mouth. Within fifteen to thirty minutes the carbon had entirely disappeared, except in one case of great interest, where a small bit, which had lodged above a protruding lymphoid nodule, was still present after one hour. This illustrates the importance of anatomical variations in producing exceptions to the general rule.

Experiment 6. The fate of carbon particles placed on the tonsil: In this experiment the applications were very satisfactory. It was easy to spread the charcoal and it adhered firmly. Except in a few cases of very large tonsils, there was no spread by contact to adjacent areas of tongue or pillars. *The carbon remained on the tonsil practically unchanged during the two hour period of observation.* None was seen after twenty-four hours. Occasionally a few particles seeped down into the glossopharyngeal crevice. Its final removal seemed to be effected in this manner.

Comment on Experiment 6: The tonsil observations were of particular interest. It is generally supposed that the tonsil is a converging point and site of collection for bacteria entering the mouth. These experiments show that the tonsil is very effectively protected and that particles are only unusually lodged on them. *However, when particles become deposited on the tonsils they remain out of the track of the mouth currents, and disappear very gradually*, by means of currents which carry them, not into the mouth cavity, but into the pharynx and oesophagus.

GENERAL SUMMARY

The general result of these experiments, then, is as follows: In the first place, there is a marked tendency for foreign particles to adhere to the mucous surfaces. This seems to be due to the irregular, polymorphous architecture of the parts, with numerous crevices in the mucous membrane, plus the adhesive qualities of the overlying layer of mucus. Having once adhered in this way, there seems to be little or no tendency for the particles to spread at large over the mouth, but they are removed in an orderly and uniform manner. Inasmuch as there is no ciliated epithelium in the mouth, the presumption is that this removal is due to suction currents set up by the muscular masses which make up the lips, cheeks, tongue, and pharynx. The general path of removal is by direct spread to the rear. *There is no forward dissemination.* The paths from the tongue, sublingual space, and palate all converge at the base of the tongue. The faucial tonsils, protected by the pillars, occupy a position which is out of the way of these currents, so that under normal conditions particles deposited in the mouth are swept past them. *Once lodged on the tonsil, however, the particles remain relatively stagnant.* Particles which fail to adhere are removed with great rapidity by the flushing action of the saliva, but are carried along essentially the same paths.

In general, it may be said that the carbon was removed in from fifteen to thirty minutes. It is of interest and importance, however, that numerous exceptions occurred to this rule, always in the way of mechanical lodgment in a crevice in the mucous membrane.

Inasmuch as the normal "resting" conditions are in actual life constantly interfered with by chewing, eating, and drinking, it seemed of interest to note in what way the above experiment could be modified by swallowing fluid after inoculation with carbon particles. The following procedure was therefore adopted: After placing the charcoal on the various sites the subject was instructed to drink a glass of water, taking it rapidly but in small sips.

Experiment 7. Carbon was placed on the anterior dorsum of the tongue and a glass of water was immediately taken. *Result:* A few superficial particles which were not adherent to the mucus were immediately washed away, but the main mass of the material was entirely unaffected and was removed as in experiment 1.

Experiment 8. Same as experiment 7, except that application was made on the hard palate. *Result:* All superficial nonadherent particles were promptly removed. A stippling of particles remained which was removed as in experiment 2.

Experiment 9. Same as experiment 7, except that application was made on the upper pharynx. *Result:* No apparent removal by the ingested fluid.

Experiment 10. Same as experiment 7, except that application was made on the tonsil. *Result:* No apparent removal by ingested fluid.

Summary of experiments 7 to 10. When fluid was taken immediately after placing charcoal on the various sites, any particles on the surface of the mass which were not well in contact with the mucus were promptly removed. The particles actually in contact with the mucous membrane, however, were apparently unaffected by the ingested fluid and disappeared according to the conditions found in experiments 1 to 6.

Experiment 11. A thick suspension of powdered charcoal in water was prepared. It was of the consistency of thin paste. The individual examined took a large swallow of this material. The distribution of the carbon particles was determined by inspection. This test was performed on four people. It was found that the dorsum and lateral margins of the tongue were uniformly covered with the charcoal particles. The cheeks and palate were marked, but to a less extent. The sublingual space showed no carbon particles, nor was there any marking of the pharynx, save in one case when a spot 1 cm. in diameter was discolored by direct contact with the tongue. In two of the four cases the tonsils were entirely free from carbon particles. In two others whose tonsils were very prominent a few particles adhered.

Experiment 12. A similar experiment was performed with a deep blue aqueous solution of methylene blue. The results corresponded with those of experiment 11. The tongue was intensely stained, the palate and cheeks to a less extent. The sublingual space was not stained in any of the four cases examined, nor was the pharyngeal wall. In two cases there was a slight staining of portions of the tonsil, while in the other two the tonsil had apparently not been touched by the dye.

In summary, then, in the process of swallowing, fluids seem to be forced or sucked back through the mouth and squirted down the oesophagus without touching the upper part of the pharyngeal wall. The tonsil on the whole is protected from contact with the stream of fluid, although anatomical variations in the size of the tonsils and in the disposition of the pillars of the fauces will in some cases vary this result.

DISCUSSION

The experiments described were undertaken because previous bacteriological observations had indicated that microörganisms, introduced into the mouth, were rapidly removed, and that bacteria located in a focus such as the tonsil were not uniformly spread throughout the mouth cavity. It seemed likely, therefore, that there was some definite mechanism for promptly removing such foreign bacteria in an orderly way. The present experiments with foreign particles crudely duplicate what might be expected to obtain in the case of the deposition of bacteria. They show, first, that such particles for the most part tend to be anchored in the protective mucus layer, and that they are subsequently rapidly and directly removed by a series of suction currents. Obvious exceptions in regard to the speed of removal occur, owing to anatomical peculiarities and variations. The most significant finding, however, is in connection with the tonsils. Our idea had been (and we believe it to be generally held) that these structures were a collecting place for foreign bacteria which enter the mouth. The present experiments show that the tonsils are very well protected from contamination because of their situation behind the anterior pillars, and because of the course of the suction currents, but that when in some way foreign particles do lodge on them such particles remain stagnant for a considerable length of time.

In summary, then, we have here additional evidence of the protective mechanism which rids the mouth of foreign bacteria. That this mechanism frequently fails under unusual or abnormal conditions is obvious, but when one speculates on the degree of probable infection which would exist without it, it seems remarkably efficient.

In a subsequent paper similar experiments, with bacteria as a test-substance, will be reported.

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RESISTANCE TO TUBERCULOSIS[1]

AND ITS RELATION TO ANTITUBERCULOSIS MEASURES

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It is now well understood that our efforts to prevent tuberculosis must proceed along two main lines. The first aims to do away with infection, to break the contact that is so frequently established between human beings and tubercle bacilli at large. The second is to keep quiescent the infection which most men harbor within themselves.

It was the best opinion, not long ago, that only the sick with tuberculosis were infected, and that the event of infection—the fact that bacilli "took hold" and set up lesion—was determined by what was called the "resistance" of the recipient at the time of infection. A good resistance, so many maintained or implied, would permit no infection, even though germs were taken into the body. But after we became acquainted with the fact that nearly all human beings become infected, under any and all circumstances, we had to assume that initial or native resistance to tuberculous infection is more or less on a par with resistance to infection with measles; that everyone exposed, however slightly, will exhibit some evidence of contact with the virus; that there is really no complete native barrier to tubercle bacilli.

Under these circumstances, it followed that we have had to explain why the great majority of mankind keep their infection in abeyance, or, as is more usually ventured, why tuberculosis patients fall ill and why the manifestly ill show such great variations in the intensity and progressiveness of their disease. It is plain that satisfactory information on these questions would put us in a better position to fight tuberculosis; for we could then institute measures to remove obviable causative factors of disease, imperfect though these might be, involving, as they probably would, mass action and application of public health principles throughout the entire body of a citizenry which, never any too well informed, bade fair to be only partially responsive.

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[1] Elaboration of an address delivered at the Convention of the Virginia Tuberculosis Association, Richmond, Virginia, October 7, 1921.

In accounting for the well known variability of behavior of established tuberculous infection most authors have resorted to the catchword resistance. There can be little doubt that only too many have used the term without defining what they mean by resistance or trying to make plain how resistance is influenced or how its variations bring about observable fluctuations of tuberculosis. It delays, rather than advances, our knowledge of tuberculosis to assert offhand that a person develops tuberculosis because his resistance is lowered, unless we can prove that a diminution of resistance precedes the outbreak of tuberculosis; or that disease is progressing because of a lack of resistance, unless we can show that this attribute is absent or unusually slight: for, as a matter of fact, frank tuberculosis may follow trauma or sudden, excessive physical strain under such conditions that we cannot imagine any alteration of resistance to have entered as a causative factor; or severity of clinical symptoms and subsequent course of disease may turn on such factors as the points of focalization of bacilli, and where infection or reinfection may lodge must often be fortuitous, or, at any rate, independent of anything that we can conceive of as resistance; and, in this connection, it is as certain as can be that we are able to show by experiment that a tuberculous animal's resistance, immunity, to reinfection increases as its disease progresses and its symptoms are becoming more marked.

But all this is anticipating my thesis. At this place I would repeat and emphasize the plea, which I have frequently made, that we use the term resistance advisedly and that we never indulge in it unless we have some exact or concrete idea of what we mean and are talking about.

There are many factors which must influence the course of tuberculous infection yet which, by no exercise of logical reasoning, may be comprehended under a proper concept of bodily or organic resistance to it.

Among these is the element of the focalization of infection to which I adverted a moment ago. Both the immediate and remote results of any infection may be markedly influenced by the *loci* of infection. Everything else being equal, a lesion in midlung or immediately adjacent to a large blood vessel is of more moment than an exactly similar one at the apex or at a distance from larger vascular or lymphatic trunks. Two men may have identical resistances and identical infections in identical spots,—in a lymph node, say. Both lesions may shed a few bacilli into neighboring blood vessels at the same time. But in one case these germs may make their way to the meninges to set up a rapidly fatal tuberculosis, while in the other they may go to peripheral muscles to produce no appreciable effect. The progressiveness of tuberculosis is, in almost every instance, in large part a reflection of the metastasizing events which followed an original solitary lesion; and these successive eruptions of tubercles, so far as their localization is concerned, will be governed by factors which we cannot imagine as having anything to do with resistance,—factors which we must call accidental, factors which will comprehend original anatomic localization, avenues of spread, character of metastasizing material (amount, consistence, etc.), physiological activity of the host at the time of eruption, and so on. For all we know, these factors may be the most decisive of all in determining the variable course of tuberculosis, yet they are seldom given any attention.

It is encouraging that a growing acquaintance with the processes of tuberculo-immunity is introducing more precision into discussions which may involve the phenomenon of resistance. But it is also only too apparent that frequently a certain terminology is bandied about with a vagueness and a freedom which could hardly withstand definition and analysis. We read much about what happens—to patients, to groups or to races of people—because their resistance or their antibodies are raised or depressed by various causes—by fresh or foul air, by good food or a lack of it, by hygienic or vicious habits or modes of living. Seldom is any proof brought to bear that any variation of resistance contributed to the event: less seldom is it shown that "antibodies" have turned the scale, one way or the other: indeed, practically never are these antibodies demonstrated as having any existence in the circumstances. There are only too many of these explanations of the effects of tuberculosis which sound well yet mean nothing, and which, because they resolve really complicated effects into factors which are easily understood yet have no real existence in the case, exert a soporific effect, not only on their sponsors but on the scientific curiosity of the latters' auditors as well.

As it happens, there are such things as tuberculosis "antibodies;" there is a specific immunity to tuberculosis; there is real resistance to tuberculosis. And it shall be the purpose of this address to pass in review, with necessary brevity, factors and conditions which may legitimately be regarded as offering resistance to infection by tubercle bacilli and to the further progress of infection; and to touch, as well, upon some circumstances which may influence and modify these elements of resistance, and thus bring about the variegated background of tuberculosis with which we are familiar. I should like also, in passing, to point out what directions our preventive measures must take, in so far as they are to be based upon our best knowledge of resistance.

If we view the subject broadly, we are at once struck by the fact that many elements are at work in resisting tuberculous infection and its development. There are checks and barriers to infection and its spread at the portals of entry and along the avenues of bacillary dissemination; there are anatomic tissue reactions which serve to fix the bacilli and restrain their activities; and there are newly acquired attributes of specific immunity which operate in a similar manner.

Tuberculosis is essentially a lymphatic infection. Entering by digestive tract, the germs penetrate buccal, pharyngeal or intestinal mucosa, and come at once within the domain of the lymphatic system. In very many instances they pass immediately into lymphoid tissue like the tonsils or enteric follicles. If they are carried further into the body, always by lymphatic paths, they are soon intercepted by lymph nodes which are distributed with particular profusion close to portals of entry.

Bacilli from without which gain any part of the respiratory tract in the nontuberculous young are for the most part similarly carried to lymphoid tissue,—to the deep cervical nodes or the tracheobronchials. Those again which come to the lung by the blood from foci elsewhere in the body tend in early life to be carried out of the blood vessels into the lymphatic network of the lung and proceed by way of this to the tracheobronchial nodes.

It happens, therefore, that the ordinary early infections of life, which everyone to-day acquires, are localized in lymph nodes, usually the submaxillaries or deep cervicals, the tracheobronchials and the mesenterics. It happens also that when disease manifests itself in early life, it does so most frequently in these nodes or, in a very large proportion of cases of extralymphatic disease, its origin can be traced to these nodes.

What is significant is that in the great majority of infections—fully 90 per cent—the lymph nodes are competent in restraining the infection and keeping it quiescent. In experimental work I have long been tremendously impressed by the great resistance which the lymph nodes offer to the spread of infection, and particularly to the development of progressive and florid disease within themselves. In guinea pigs, unless the nodes are receiving large and continuous doses of virulent bacilli from more superficial foci which they drain, they will keep under control astonishing amounts of infection without becoming markedly diseased. The average picture is tumefaction, with caseation which is well balanced by sclerosis; to an extent, indeed, that, if we consider all nodes in the body, sclerosis usually gains the upper hand and comparative healing is the result. When infection seizes upon the smaller intravisceral collections of lymphatic tissue, which are not true nodes, as in the spleen, the result is usually different; for it is in these places that we are accustomed to find infection developing and progressing.

The more I observe infection and disease in human beings and in animals of experiment, the more I am impressed with the function of the lymph nodes as instruments of high resistance to the unchecked spread of tuberculosis. A sound and competent lymphatic system is of great importance as a defense against tuberculosis. Unobstructed lymphatic paths, permitting free and easy passage to lymph nodes, will allow focalization in the nodes themselves where bacilli are comparatively harmless, rather than in more peripheral visceral tissues, where conditions are more favorable for their development and extension. Lymph nodes which are subject to irritation not infrequently reveal the outbreak of frank tuberculosis from quiescent foci with a positiveness that cannot be misunderstood. The cases of clinical tuberculous lymphadenitis of the neck nodes which follow scarlet fever or tonsillitis or chronic tonsillar inflammation are numerous, as are those of the pulmonary root after measles. Chronic foci of buccal or pharyngeal inflammation exerting their effects by subsidiary congestion or inflammation of the neck nodes, which in turn light up old latent tuberculous foci in the latter, are frequently found in connection with the appearance of cervical tuberculous lymphadenitis.

What happens in these cases is plain. Tubercle may be well invested for years in lymph nodes, which act as resisting organs so long as they are competent; but acute or chronic irritation from peripheral areas which they drain brings about abnormal anatomic and physiological conditions which permit the renewed development and spread of infection. Rational and scientific measures of prevention of tuberculosis must aim, particularly in children, at the more general attainment of healthy mouths and throats and the more complete restriction and control of all constitutional infections, which bring in their train local or generalized involvement of lymph nodes, of shorter or longer duration.

There is a striking unanimity in the reports of medical examiners, to the effect that diseased teeth, hypertrophied or inflamed tonsils, and adenoid growths in the nasopharynx make up by far the largest number of pathological changes to be observed in children. There is something in our mode of life—something yet to be discovered—which operates on a scale to make these disabilities seem almost the normal lot of children under present conditions. Given the proper peripheral irritation in mouth or throat acting *at the right time* on the proper tuberculous lesion in neck node, and manifest tuberculosis develops, or bacilli may be mobilized and carried to bone and joint, to lung and tracheobronchial node, or even to meninges, there to set up reinfection and disease. Even though the conditions of tuberculous infection, *per se*, remained perfectly static, we could expect a tremendous decline in tuberculous morbidity of children—and, as an indirect consequence, of adults—if all mouths and throats were put in a healthy state and if measles, diphtheria, common colds, etc., were wiped out. In brief, a healthy lymphatic system means a good defense against developing tuberculosis; all burdens laid upon it by nonspecific and vicarious irritation lower the threshold to tuberculosis and favor its development in the lymph nodes and its spread from these to more central parts of the body.

A few moments ago I mentioned the conversion of well invested tubercle to lesion which entered upon a cycle of renewed development and extension of infection. This transformation is one which may occur under the stress of many influences and one too which marks the change of a defensive or resisting mechanism to a menacing structure which, for a time at least, may exhibit few features of protection. It embraces several phases of resistance and its opposite, which may profitably engage our attention.

It has become trite to point out that the peculiar anatomic formation of tubercle with which the body meets the access of tubercle bacilli is *intrinsically* (though not completely) the result of reaction on the part of tissues to foreign bodies. Nevertheless, this truth must again be stressed in this place, so that its full significance may not be overlooked.

Tubercles are thoroughly avascular, globoid structures, built up by the proliferation or new growth of cells, in response to irritation by foreign bodies, in this instance highly resistant tubercle bacilli. The spherical mass of newly formed cells surrounds the bacilli and, as it develops, becomes permeated with cells of another nature, leucocytes, which wander in from outside of the mass. Developing further, the outer layers of the proliferated cells of the tubercle become flattened and throw out fibrils, in a way that ultimately leads to the formation of a compact sclerotic envelope if the process continues without interruption. In most cases, in first infections in which we have reason to assume that the number of bacilli is usually small, it does so continue. In fact, our data of the universality of infection and of postmortem observations make it appear that this is the more usual and more normal course of tubercle under natural conditions of infection; that is, that bacilli entering the body are invested by cells which become transformed into layers of fibrous tissue between them and adjacent normal tissue.

The net result of this process is the interposition of an envelope which interns and walls off the bacilli. It is an exhibition of resistance, of a defensive or protective mechanism. It may be thoroughly and permanently effective, as, for instance, when the periphery of the tubercle is very dense and compact and practically impervious, and the bacilli in the interior die. It may be competent for so long a period that we may call it permanent, even though bacilli remain alive inside, as we may observe when we find bacilli with perhaps some caseous or calcareous material enclosed within thick and almost gristled wall—I have seen a tubercle with caseocalcareous centre, and wall of almost rubbery consistence a quarter-inch thick by measurement. It may be only relatively and transitorily protective, as we shall see in a moment. But the point to remember is that, even though many of our symptoms of illness arise from the anatomic and physiological disturbances set up by the several metamorphoses of tubercle, the tubercle is always a defensive structure: within it is always the function of resistance.

And now arises the fair question: Why don't all tubercles resist completely and permanently?—for we have said that most do. Or, what operates to break down the defensive properties of tubercle? What whips them up to renewed development, to growth, to extension, to scatter their harmful contents further and broadcast? It is this matter of the breakdown of tubercular resistance which we would now look into.

Altogether apart from the character and number of bacilli which always play their part at any particular time, the character and effects of tubercles will always be influenced by all activities that go on in their neighborhood; that is, they will be so influenced as long as they are in an anatomic state which is subject to change and up to and until that time when they may have been completely converted into scar tissue, when their career can be said to have finished. But, until this event occurs, we may say with certainty that a relation of potential "give and take" exists between them and surrounding structures. Under the proper physiological conditions they yield something of themselves to the tissues nearby and through these to the body at large, while they at the same time receive something from the latter. This interchange will vary with the degree of investment that involves the lesions and with the physiological activities of functioning tissues which enclose the tubercles. Everything else being equal, good peripheral sclerosis will make for quiescence of tubercle under ordinary conditions and will withstand relatively great and violent fluctuations and changes, circulatory and otherwise, of the involved organs. Given tubercular investment of any competence, and relative rest of the involved part will favor tuberculous inactivity, while anything which brings about more active circulation and function promotes the conversion of latent into frank foci or the increase of vigor of already active foci.

Let us try to be still more explicit. What, at bottom, do we mean by quiescence or latency or inactivity of foci; or by frankness and activity? Men may disagree on details that would define the shadowy line that not infrequently distinguishes quiescence from activity; but there can be little dispute on the general proposition that tuberculous foci which do not give rise to symptoms in people who are living their normal life are quiescent *under the circumstances*, while those which produce symptoms are active *under the circumstances*. I say *under the circumstances*, because by strain or overwork we can bring on symptoms in many people who are normally without them, and thus, for the time being, arouse quiescent foci to activity, just as by rest or more complete relief from strain we can rid patients of all symptoms of illness, and during this time may consider their disease as relatively inactive. Quiescence and activity of lesion reflect the bodily activity of many patients with exquisite delicacy. In practice, we must, however, have some standards, and I doubt whether any better working rule or criterion has been found than to base our estimations on what happens to patients who are pursuing their normal lives.

At any rate, in estimating quiescence and activity the things that count are not so much the *signs* of extension or retrogression of lesion, *considered purely by themselves*, nor the local symptoms of cough, sputum or diminished function, which may be the residua of healed or arrested lesions, as they are the constitutional symptoms of fatigue, malaise, fever, irritable pulse, etc. These constitutional symptoms are, without exception, the expressions of an intoxication which follows the exit from tuberculous foci of substances which we will not stop to define and which are taken up by the circulation in the neighborhood and distributed throughout the body. These are the symptoms which almost always usher in clinical tuberculosis, which announce the "breakdown of resistance" if one wishes to view the case in this light, which by variations in intensity and duration furnish, rightly or wrongly, the clinician with his scale of measurement of resistance.

And whether these symptoms will be absent or present, or more or less marked, will in the ordinary case depend upon the nature of the tuberculous foci; on whether the foci are well or poorly invested, and thus relatively closed or open to the heightened respiratory and circulatory activity which follows increased physiological demands upon the body or the involved part, and thus in turn permit of less or greater exit and absorption of focal materials.

More concretely, we may enumerate many events which would influence the competence and integrity of the barrier which protects the body from the deleterious substances in quiescent tuberculous foci; events which contribute to the "opening," as it were, of these tubercles, thus promoting the absorption of poisonous materials and the mobilization and further dissemination of enclosed bacilli; events which produce those physiological effects that overcome the defensive capacities of a mechanical, anatomic barrier. Intercurrent diseases of many kinds, particularly those which bring about congestion and inflammation and thus enhance the activities of the blood and lymph circulations; physical and emotional stresses which contribute to the same physiological result; abnormal metabolism, which may have the same effect—even that resulting from overfeeding, as is suggested by McCann's recent work; in short, to repeat it almost *ad nauseam*, anything which puts physiological strain upon a part is a potential spur to quiescent tuberculous foci in that part, a possible sapper of the mechanical resistance to symptomatic disease and bacillary spread afforded by anatomic tubercle.

It is, of course, self-evident that in the development of clinical tuberculosis, another fortuitous element, namely, the time at and during which tuberculotrophic stresses are at work, is of prime moment. We have said that anatomically no tuberculous process can be considered static until it is thoroughly healed. In its development and its retrogression it will pass through cycles of pathological changes, which would offer many grades and degrees of resistance to the same strain, if this were a fixed and uniform thing. So it will matter much when, in the course of its development, any given tubercle comes under the influence of an intercurrent inflammation, or pregnancy, or any unusal experience on the part of its possessor. A child, for instance, may suffer an attack of measles at a time when whatever tubercle it harbors is well sclerosed—at least well enough to withstand the deleterious effects of the infection at the time; and the measles passes without sequela. But the measles may also attack a child not long after the event of tuberculous infection or slight and inappreciable extension of infection or reinfection, when foci of tubercle are not so well invested and are more open to the influence of measles: the result in this case may be what many physicians have observed, namely, the appearance of clinical tuberculosis after measles. Why tuberculosis follows certain experiences in some people and fails to come to the front in others who have gone through the same experiences is undoubtedly often due to the fact that the former were more unfortunate as regards the time when they went through unusual stress.

This analysis of a very prominent phase of resistance to tuberculosis teaches us that those preventive measures *are fundamentally sound* which aim to reduce the unusual and useless stresses and hazards of life, whether by bringing home to the individual consciousness the risks of unnecessary overstrain, dissipation and exposure, or, by more public effort, to ameliorate the conditions under which a large portion of our people live, or by general hygienic measures to reduce the sum total of improper living conditions, with their consequent preventable diseases of many kinds. They square with conceptions of the development of tuberculosis, of the reduction of resistance to it, which we have every reason to believe are true, basically and in outline, impossible though it may be to fill in all details or explain every sequential step in every given case. The fact that not all people, or even most of them, who live under conditions or undergo experiences which are provocative of clinical tuberculosis, do not develop the disease does not weaken one jot the argument that certain environmental factors promote and actually bring on tuberculosis: it weakens it no more than would a comparable contention, that alcohol is not the cause of delirium tremens because most users of alcohol do not get delirium tremens, make us question the rôle of alcohol in the production of delirium tremens. Tuberculosis is a striking example of those affections which are brought into being by the coöperation and combination of several or many contributory causes;

just as, on occasion—when an habitué is stricken with pneumonia or other acute disease—even delirium tremens may be. If anything is certain, it is that the curve of incidence of morbid tuberculosis will run closely parallel with comparative deprivation of the means of subsistence and all the overstrain, exposure, faulty living and misery which accompany inability to live comfortably—granted always, of course, that tubercle is a universal infection in any community in question—and understood, also, that fixed monetary incomes must not be our economic standard, inasmuch as the same annual return may buy comfort for the peasant of Bulgaria yet spell poverty for the inhabitant of New York City.

During the last twenty years we have been learning more and more about a third type of resistance to tuberculosis. This is specific immunity. Specific immunity is a form of increased resistance which is acquired by all animals which become infected with tubercle bacilli. It can be attained only by infection, as is the case with the immunity of the exanthematous fevers; but it is unlike the latter in that, as infection heals and disappears, immunity diminishes and dies out. Tuberculo-immunity is therefore more comparable to that which follows syphilitic infection, inasmuch as it is well known that as a person's serum ceases to give a positive Wassermann reaction, he can again be infected with characteristic chancre.

After tuberculous infection deep seated changes go on in the body. Among the most remarkable is the circumstance that the tissues take on an entirely new reacting capacity to tubercle bacilli. While the tissues of the normal, nontuberculous organism react to first contact with tubercle bacilli by the slow and indolent formation of nodular tubercle, a structure made up, as we have seen, *essentially* of proliferated cells, the tissues of a tuberculously infected animal will react much more rapidly to the reimplantation of bacilli in new places; in fact, almost immediately, and with an inflammation which may be quickly followed or accompanied after a few days by real proliferative, tubercular changes. This new reacting power is denominated tissue hypersensitiveness or *allergy*.

The manifestations of allergy may vary from the slightest and most transient inflammatory traces to violent haemorrhagic inflammation with rapid necrosis. Its vigor will depend upon two factors, namely, the degree of hypersensitiveness and the numbers of bacilli brought to bear at a point at a given time. When numbers of bacilli are relatively few, they are rapidly hemmed in by the accelerated tissue reaction, kept from disseminating and proceeding further into the body, and very often destroyed in a short time: all this without symptoms of illness in the host. But when numbers of bacilli are great and allergy is high, the host may be made acutely ill by the violence of the tissue reaction. Cases of acute tuberculous pneumonia are invariably those in which an already infected person has received a sudden accession of a large amount of tuberculous material—practically always from within—into his lung. What now happens is that a person falls ill because of his hypersensitiveness: and, although such a patient may seem to the clinician to exhibit low resistance because of the gravity of his illness, the fact is that he is so very ill because he is immune. For it is of the greatest importance to understand—what can be easily proved experimentally—that a normal, nontuberculous animal will tolerate enormous inoculations of living, virulent tubercle bacilli without being made ill thereby for several weeks, when early lesion is at last becoming manifest, while a slightly infected and therefore immune animal will fall acutely ill a few hours after reinfection (by the blood) of relatively small doses of living bacilli.

Such are a few features of tissue allergy and specific immunity to tubercle bacilli. As it works out in nature, the case may be stated something as follows:

Most infections from without, to which human beings are exposed, represent no doubt contacts with relatively few bacilli; and most human beings are exposed to infection, not once, but several or many times. First infection usually "takes;" very few bacilli are necessary and the body's native way of meeting the infection is to react slowly with tubercle. Every infected person becomes hypersensitive in varying degree and relatively immune to reinfection, whether from within or without. As long as first infection or internal reinfections from first infection persist, hypersensitiveness and immunity will remain in fluctuating degree: they will increase as infection progresses, become less as it tends to die out and disappear completely if it heals and lesions become sterile. There is no doubt that many persons, who never develop clinical tuberculosis, never rid themselves of their first infection: there can also be hardly any doubt that in many others it disappears and that fresh infections from without renew hypersensitiveness and immunity.

Because of his immunity an infected person will resist reinfections from without which would undoubtedly produce lesion in the normal, nontuberculous person. Ordinary contact with tubercle bacilli is relatively harmless for him, so long as he remains infected; but it must be clearly understood that no known tuberculo-immunity is of so high a competence that it can withstand every grade of exposure to infection.

But it is in relation to one's own infection,—to the possibilities of extension and dissemination from it and to the manifold pathological changes which it may produce,—that allergy and immunity are of tremendous importance in resistance. It is obvious that implantations of infection from foci may comprise any number of bacilli, from single germs to enormous numbers. It is very likely true that these larger numbers of bacilli are much more often concerned in these reimplantations than in infections from without; it is beyond question that practically all widespread focalizations of bacilli originate from foci within the body. *In other words, the course of most tuberculous infections is governed much more by the successive events of autogenous or endogenous infection than by single or repeated infections from without;* for in the former the chances of drainage are very much greater. And in this series of events, specific immunity and hypersensitiveness play, we may be sure, an almost preponderant rôle, and supplement the mechanical defense erected by anatomic tubercle.

We have stated several times that the normal susceptible animal, including man, is natively open to infection (and the production of lesion) by a very few, perhaps one, living bacilli. If then, this native reaction were not changed by the event of infection, if, in other words, no specific immunity were acquired, the infected animal would respond to every new localization of metastasized bacilli with the same slow and lazy proliferation of tubercle with which it reacted to first infection from without. And since we know how rapidly and widely unfixed tubercle bacilli can spread throughout the body, we would expect that under these circumstances most cases of tuberculosis would acquire an infection, which would be very widely disseminated soon after the intake of bacilli from without.

But it is specific immunity and allergy which prevent the permanent focalization of small and moderate numbers of bacilli and operate always in a way that tends to confine the activities of the bacilli to one or a few points. Within a period which varies from five or six days to four weeks after infection the body is becoming allergic and immune: and, while the tissues are building up tubercle at the point of initial localization of bacilli, the tissues are acquiring the property to react with great celerity and with inflammation, if need be, to all which may lodge in new places. It results that those germs which may be conveyed out of the young and imperfectly formed tubercles to other parts of the body meet with the much more active resistance of specific immunity, and are either done away with or given a check for the time being. All this can be worked out with precision on the animal of experiment.

The restraint is not always complete. If the immune process does not entirely destroy the bacilli, the few that remain go on to produce new lesion, subject to all the influences and eventualities we have already mentioned. But the effect of this relative immunity is always plainly an inhibitive action on bacillary spread.

The spectacular effects which follow the discharge of large amounts of tuberculous material from existing foci are nevertheless conservative and expressions of resistance, even though they endanger the life of the patient. The clinician is accustomed to interpret resistance in terms of symptomatic severity: to him stormy illness appears an evidence of lowered resistance against the invading parasite. But the experimental pathologist must score resistance on the basis of the issue of controlled end-effects: and he will find that in tuberculosis the animal which rapidly responds to infection with illness is that which resists infection the best. You will observe this seeming paradox every time you make the following experiment: Infect a number of rabbits or guinea pigs with living tubercle bacilli of low virulence, which will give them slight, localized, nonprogressive tubercle. Four weeks later, after allergy and immunity are well established, reinfect these with virulent bacilli introduced by a vein, and at the same time infect in exactly similar manner a control series of normal rabbits or guinea pigs for the first time. You will find that the latter, receiving a first infection, will not exhibit the least symptom from the operation. The reinfected animals will fall acutely ill within a few hours. Some of them may die within the next day or two, when autopsy will bring to light pneumonic patches in the lungs and inflammations in other organs where tubercle bacilli have embolized. The survivors will soon recover from their acute illness and live indefinitely; and, if they are killed and examined six months and more later, their organs will be comparatively free from tubercle. But the originally normal controls, which received only a single infection of virulent bacilli and withstood this without acute illness, will develop progressive tuberculosis and die of it within two or three months.

Here we have a situation which we may roughly characterize as follows: The immunity of the infected cost some of them their lives though it spared the survivors from progressive tuberculosis. The lack of immunity of the normals spared these from acute illness though it cost all of them their lives from progressive tuberculosis later.

The acute tuberculous pneumonias of human beings do serve to limit the field of activity of large numbers of mobilized bacilli, even though they make the patients gravely ill: when recovered from, the disease again usually takes a chronic course, for a shorter or longer time, or becomes arrested. If there had been no pneumonia, these patients would, in every case, have gone on to rapidly progressive tuberculosis, extending fulminantly to all parts of the body.

If allergy and specific immunity were immutable properties and proof against outside influences, the story of tuberculous infection and disease would be very different from the one we all know. But just as we saw that the resisting elements of anatomic tubercle and lymph node focalization may be decisively modified by many specific and nonspecific factors, so we shall find it with these attributes.

We have referred several times to the fact that both immunity and allergy fluctuate with the amount and character of the underlying infection: they are more active as infection progresses, less vigorous as it retreats, absent if it heals completely with bacillary sterilization and, at any time, sharply heightened by reinfection.

They are also markedly affected by more external and nonspecific factors. It has been abundantly proved that allergy is depressed and even abolished by infections such as influenza and measles, by fever from various causes, and by pregnancy. It is a fair prediction that further investigation will show it to be similarly modified by fatigue, malnutrition, exposure to undue heat and cold, in fact, by anything which depresses normal bodily function. I have in mind a known tuberculous but profoundly anaemic child, in the service of Dr. Howland at the Johns Hopkins Hospital, who reacted negatively to repeated Pirquet test, but strongly after a transfusion had been done.

Many bodily conditions, therefore, which are the effects of faulty living and hygiene, will likely reduce allergy and, as a consequence, a specific immunity. So again we find that our present methods of tuberculosis prevention, aimed to improve living conditions and to reduce the incidence of many collateral diseases, are in harmony with our scientific knowledge of specific immunity, a third phase of resistance.

This discussion of resistance has, of necessity, been very incomplete. But it should point out what is only too often lost sight of,—that the outbreak of clinical tuberculosis in any case is the culmination of many contributory factors and events. In every case, no matter what the issue, some resistance or resistances are at work; and it is the interplay of the resistance and the experiences of the individual which determines the outcome and, after what is usually a protracted period, results in anatomic and clinical complexes which are as numerous almost and diverse as the infected themselves.

Underneath it all there are no doubt other partial determinants which have a share in moulding the final result. Everything that we observe suggests that human beings vary greatly in their reacting capacity to irritants, in their vigor of immune response, in lymphatic function and in that harmonious correlation of organic functions which we postulate as normal. They are different in these respects because they were born different: inheritance endowed their tissues with capabilities which are not exactly alike in any two persons. Therefore, the effects of these differences must also, in the last analysis, enter into the ultimate result of tuberculous infection. But these variations have thus far been so intangible and so involved that they have defied scientific analysis and formulation.

After all, it is encouraging to reflect that whatever the future may disclose, however we may from time to time be obliged to change and modify our antituberculosis plans, these, in design, are in harmony and are keeping step with our best authenticated knowledge and are thus proceeding on a rational and scientific basis. The difficulties—the faults—of our measures to combat tuberculosis do not lie so much in the latters' design. They originate and grow large in their execution,—in getting the people to see and to act. And our future course, it seems to me, is plain. It is to intensify and expand our present activities, to go along without letup, keeping our eyes and ears on all scientific investigation which will slowly yield up the truth and transmitting this promptly and effectively to an ever-widening public. Teach your intelligent men: reach them: and they will lead the rest.

climate and travel. Besides, his several years at Saranac Lake, with its wealth of professional association, was making him keenly alive to his isolation,—for now his medical companions were necessarily few. After five years of hard work and small pecuniary reward, he once more began to cast eyes toward Saranac Lake.

He found an opening and in the spring of 1915 returned with his family to settle there. He fitted readily into the way of the place, sought out a desk at the Saranac Laboratory to study, and opened an office for practice. For a year or two practice came slowly, and the laboratory engaged much of his time, an opportunity which he used to make one or two worthy contributions to tuberculosis. Because of his physical condition the Canadian Army would not accept his medical services, when he offered to enlist. The absence of six Saranac Lake physicians in the American Army threw more clinical work to Paterson; and by the time hostilities ended his reputation had grown to an extent that patients referred to him for treatment took up practically all his working hours. He had become one of our best known practitioners of tuberculosis, but there is no doubt that the study of tuberculosis lost a likely devotee in his rise toward professional distinction. Once again did the play of circumstance make the student turn artisan,—another arm of that strange Chance that put a loaded pistol into the hand of a deluded patient and aimed it at no man's enemy, innocent of injury!

Big of body, hearty in voice and manner, high and open in laughter, bluff, candid, confident in opinion, positive in its expression, Paterson was a personality,—Scotch through and through, with just a tinge of Church of England veneer. When with his crowd and all parade clothes doffed, the veneer was likely to crack and rub off. Sturdiness marked his every movement; it put heart and backbone into all who met the man and lost nothing of its influence because of a certain roughness. Had Paterson been a "smoother" man he would have gained not a friend more, yet might have lost a few. Patients and friends saw in him power, earnestness and honesty; and good nature cemented the relationship.

Since his return to Saranac Lake, Paterson had kept well and capable of hard work, and had ostensibly many years of effective work ahead of him. His death has been a horror to all of us—an event that baffles analysis and makes straight thinking impossible. It stirs the depths of every heart to most poignant sympathy for a tortured wife and bereft children. It brings, too, a realization of the cruel misfortune which has fallen upon the group of physicians which came to gather about Trudeau. They will miss Paterson. He brought strength to them. They will fill up the rank and march along.

Robert Childs Paterson was born in Montreal, on April 29, 1878, the son of Mr. and Mrs. William S. Paterson; educated at the Montreal High School and Montreal Collegiate Institute; graduated by the Faculty of Arts, McGill University, in 1898, and by the Faculty of Medicine, in 1902; a house officer and medical superintendent of the Montreal General Hospital, 1902–1904; a student at London, Freiburg, Berlin and Berne, 1904–1906; an attending physician to the Reception Hospital and to the General Hospital of Saranac Lake, and an instructor in the Trudeau School of Tuberculosis; a member of Delta Upsilon Fraternity, Canadian Medical Association, American Medical Association, National Tuberculosis Association, Association of American Pathologists and Bacteriologists, American Climatological and Clinical Association, and American Association for Thoracic Surgery; a lover of outdoor sports and a skilful participant in all that his physical handicaps allowed; the head of a peculiarly happy household; a communicant of the Protestant Episcopal Church and a member of the Parish of St. Luke, the Beloved Physician; a very active figure in the civic affairs of Saranac Lake; the author of perhaps a dozen contributions to medical literature, two of which have appeared in these pages.

A. K. K.

THOMAS WILLIS

AND HIS DE PHTHISI PULMONARI[1]

WILLIAM SNOW MILLER

From the Anatomical Laboratory of the University of Wisconsin, Madison, Wisconsin

Prologue

In the fifth edition of Gray's Anatomy, we read, "The remarkable anastomosis which exists between the branches of the carotid and vertebral arteries at the base of the brain, constitutes the Circle of Willis."

What memories these magic words recall to the physician who was a medical student one or two generations ago. The dimly lighted dissecting room with its multiplicity of odors. The constant danger of "dissecting wounds." The long and, as a rule, dry didactic lectures; dry as the bones held in the hands of the Professor. The hilarious moments just before the Professor appeared. The "passing up" of the student who was bold enough to occupy a front seat reserved for his superiors. The grand break for the door when the lecture was over. Nevertheless, few of the medical students of those days took the pains to ascertain who Willis was; where and when he lived; or if he did anything else than describe his "Circle."

Any biographical sketch of Thomas Willis must be founded on that given by Anthony à Wood in the *Athenae Oxonienses*, supplemented by the *Post-Scriptum*, prefixed to the second part of the *Pharmaceutice Rationalis* written by Willis's brother-in-law, Dr. John Fell, who became Bishop of Oxford. For this reason there must be, of necessity, a certain degree of sameness in all sketches.

Thomas Willis was born at Great Bedwyn in Wiltshire. The exact date of his birth is questionable. Wood, Munk, Adams, and the *Dictionary of National Biography* give January 27, 1621, as the date and it is the one I shall accept.

The early education of young Willis was obtained at a private Grammar School conducted by Edward Sylvester, in the parish of All Saints,

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[1] Read at the October meeting of the Wisconsin Medical History Seminary, 1921.

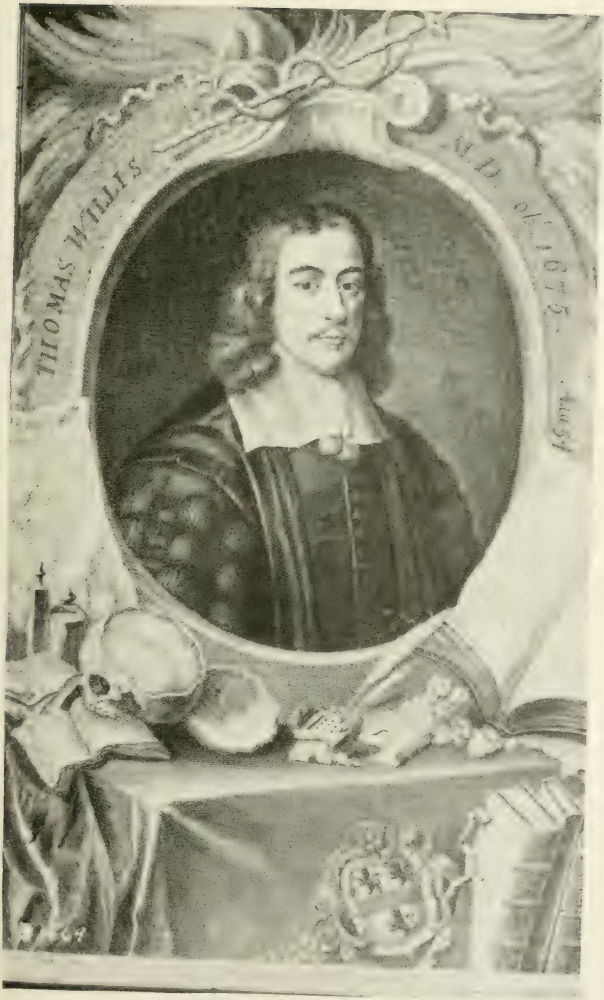

FIG. 1. THOMAS WILLIS
(1621–1675)

Oxford. In 1636 he obtained, through the patronage of Dr. Thomas Isles, a canonry in Christ Church College. He was a hard student and progressed rapidly, taking his B.A., June 19, 1639, and his M.A., June 18, 1642.

During the boyhood of Willis great changes took place in the government of England. James I died in 1625 and was succeeded by Charles I. Constant friction existed between the new king and his Parliament and in 1629 he dissolved Parliament. For the next eleven years (1629–1640) the king had the upper hand and ruled without a Parliament. These intervening years were marked with bitter strife; and finding himself without funds he summoned a Parliament, known as the Short Parliament, for it was almost immediately dissolved because it refused to vote him the money he so much desired. In the autumn of 1640 the king summoned another Parliament known as the Long Parliament, for it sat for almost two decades.

In January, 1642, the king considered himself strong enough to attack the Parliament and attempted to arrest the principal leaders. In this he failed, and when London rose in arms against him he fled to York. The king's party held York and Oxford, but the loss of the battle of Edgehill forced the king to retire to Oxford which he proceeded to fortify. Willis remained faithful to the king and formed one of the garrison of Oxford. It was during his service in the garrison that Willis began his study of medicine, and on December 18, 1645, he was graduated M.B. In 1646, Oxford surrendered to the Parliamentary forces, and Willis settled down as a practitioner in St. John Baptist's parish, Oxford. He quickly became popular and successful, Wood stating that he "was sent for far and near for his help." He did not, however, degenerate into a medical machine with only the purpose in life to accumulate money. During these busy years he found time to publish his essay on *Fermentations, Fevers, and Urines.*

Willis had already lived under three different administrations, James I, Charles I, and Cromwell; he was now to pass under a fourth, or perhaps I should say fifth, for the year following the death of Cromwell was one of pure anarchy. He saw two extremes: the reign of the pacifist James I "peace at any price" at one end, and what it eventually led to, anarchy, at the other. With the Restoration in 1660, Charles II came to the throne and the ancient constitution which declared that "the government is, and ought to be, by king, Lords and Commons" was restored. The loyalty of Willis was rewarded, for on August 25, 1660, he was made

Sedlies Professor of Natural Philosophy at Oxford and the previous occupant of the chair, Dr. Joshua Crofts, was ejected. Continuing his studies, Willis graduated Doctor of Physic, October 30, 1660. These two events added greatly to his reputation and he became the attending physician "to most of the people of quality about Oxford."

In 1645, before the civil war had reached its conclusion, a group of men in London had met and organized themselves into a society "for inquiry into natural philosophy, especially the new philosophy." The leaders in this movement were Doctors Wallis and Wilkins. By their removal to Oxford in 1648 the Society became divided into two separate societies: one at Oxford, the other at London. The Oxford society, of which Willis was a member, was the more important of the two, and held its meetings at the lodgings of Doctor Wilkins, who had become Warden of Wadham college. After the Restoration the two societies were reunited, and chartered in 1662 by Charles II as the Royal Society of London for the Promotion of Natural Knowledge. On November 18, 1663, Willis was elected a Fellow of the Royal Society, but he was not admitted until October 24, 1667, an omission which is accounted for in the Journal Book as follows: "Dr. Willis was chosen, having been forgot to be chosen again at the time when upon renewall of the charter, the Council, according to the power granted them therein, did receive and admitt into the Society such persons as had been elected afore upon the first charter." In 1664 Willis was made an Honorary Fellow of the Royal College of Physicians of London. From these elections it will be seen that his reputation as a scientist had extended beyond Oxford.

The Doctor Wallis mentioned above became Professor of Geometry at Oxford: Doctor Wilkins eventually became Bishop of Chester. There were other men, members of the Oxford group, who made a reputation for themselves in later life. Christopher Wren became the noted architect, but at that time he was a student of medicine under Willis. He invented a method of transfusion of blood from one individual to another. Another member was Robert Boyle, author of Boyle's Law. Sir William Petty, whose name is more often associated with political economy than anatomy, was in 1651 Professor of Anatomy at Oxford and a member of the group. He it was who resuscitated Ann Green, a young woman who was "hanged by the neck until she was dead" and then handed over as a perquisite to the Professor of Anatomy, who laid claim to the bodies of all criminals, for the purpose of dissection. Although the relatives of the young woman had taken a pull at the rope, before she was cut down and had jumped on her body to make sure that she was dead, Petty resuscitated her, and she lived for many years and became a respectable member of the community in which she lived. Other members of the circle of remarkable men at Oxford were Lower, Sydenham, and John Locke.

While these things were taking place Willis was not unmindful of the more materialistic side of life. On April 7, 1657, at St. Michael's, Oxford, he married Mary Fell, daughter of Doctor Samuel Fell, Dean of Christ Church, and sister of Doctor John Fell who became Bishop of Oxford. She died October 31, 1670, and was buried in Westminster Abbey. On September 1, 1672, Willis married for his second wife Elizabeth, eldest daughter of Matthew Nicholas, Dean of St. Paul, and widow of Sir William Calley.

About 1667, according to the *Post-Scriptum* noted above, Willis left Oxford and took up his residence in London. It seems probable that the friendship which existed between Willis and the Archbishop of Canterbury influenced him greatly in making this removal from Oxford, where he had a well established reputation, to London where he had to begin life over again. The venture was, however, successful and in a short time "he became so noted and so infinitely resorted to for his practice, that never any physician before went before him, or got more money yearly than he", to quote the quaint language of Wood.

Early in November 1675, "he seemed troubled with a cough (now the Epidemical Disease of the time) which (while it was thought light and inconsiderable) suddenly passed into a Pleurisie and Peripneumonia," to quote the pharaseology of the *Post-Scriptum* already mentioned. He died November 11, 1675, and was buried November 18th, in Westminster Abbey, by the side of his first wife.

The fact that Willis was essentially a medical practitioner makes his contributions to science all the more remarkable. He was assisted in his work by Richard Lower, Christopher Wren, Thomas Millington, and Edmund King; he freely acknowledged their help, but there seems to be no reason for the statement by Wood that Lower "helped or rather instructed" Willis. Foster makes a similar statement. Each of them overlooks the fact that Lower was a student under Willis and working under his direction. Nevertheless Foster admits, when speaking of his *Cerebri Anatome*, that it is a classic work. Faulty as much of Willis's reasoning seems to us, he had a working hypothesis of what we call vasomotor nerves: he had also, according to Foster, "dimly laid hold of the doctrine of reflex action." Boruttau calls Willis the "Father of Localization in that he made the first investigations to separate the functions of the brain and to locate them in different parts of the brain."

Before the time of Malpighi the lungs were supposed to be made up of bloody spume in which the air and blood were mingled. Malpighi showed by means of mercurial injections into the blood vessels of the lung that the air and blood were contained in separate systems of vessels. His idea of the structure of the lung was rather vague. All the air spaces of the lung communicated, not only with one another, but also with the connective tissue spaces. Willis carried the work a step further by injecting mercury into the bronchi rather than into the blood vessels, and proved that there was not a general intercommunication between the air spaces, but that there were definite areas marked off by connective tissue septa, each of which was supplied by a bronchial tube. His plate illustrating this arrangement is excellent and clearly shows his idea of lung structure (figure 2). His work on the superficial lymphatics of the lung is remarkable, and the plate accompanying the text is the first one in which they are adequately illustrated (figure 3).

Willis did a large amount of physiological work which must be passed over. To him we owe the first account of epidemic typhoid fever; he was the first to name and describe puerperal fever; his clinical pictures of hysteria are striking; and his differentiation of diabetes mellitus from other types is classical. He also gives good descriptions of bronchial asthma, whooping cough, and scurvy.

However interesting his treatment of these subjects may be, they must be disregarded and special mention made of his description and treatment of "Phthisis properly so called, or of a Consumption." In the following pages free use will be made of abstracts and entire paragraphs from his *De Phthisi Pulmonari*.

> A phthisis is usually defined as a pining away of the whole body, originating from ulceration of the lungs. But this is not true: because I have opened the dead bodies of many who have died of this disease, in whom the lungs were free from any ulcer, yet they were set about with little swellings (*tuberculis*), or stones, or sandy particles throughout the lung. . . . A phthisis is better defined as a withering away of the whole body arising from an ill formation of the lungs.

This shows the careful attention Willis paid to the gross pathology of the lung. The "stones" were either calcified lymph nodes or caseous

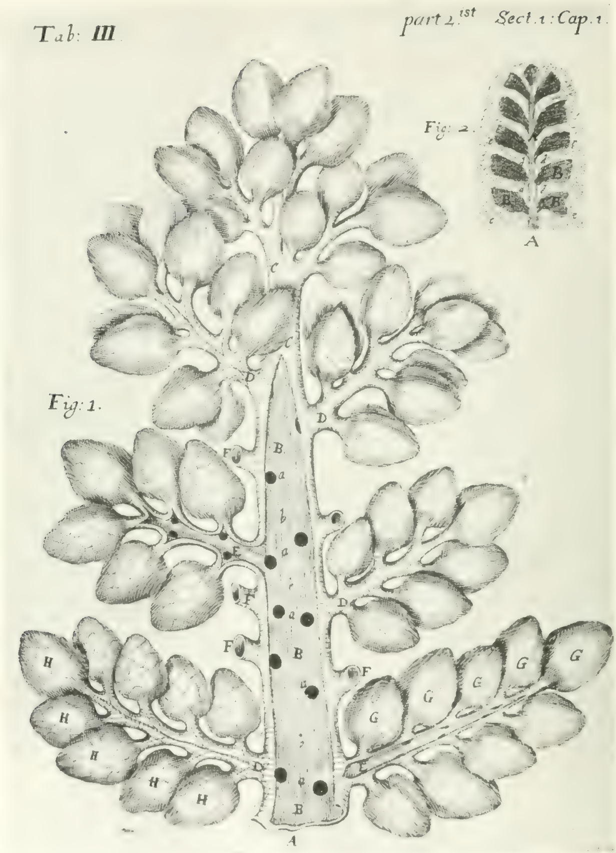

Fig. 2. A Lobe of the Lung Showing its Subdivisions

A: Main stem bronchus. *D:* Bronchus passing to the subdivisions of the lobe. *G:* The secondary or little lobes within which the "little bladders" are situated. These are arranged along the bronchus which enters the little lobe in the same manner as the little lobes are arranged along *D*.

masses which had become inspissated and later calcified by a slow deposit of calcium granules. The "sandy particles" were probably small granules of calcium deposited in the smaller masses of lymphoid tissue or in small caseous masses It is not improbable that calcification of the bronchial cartilages may have given rise to some of the "sandy particles" which his knife encountered as he cut open the lung. That these calcified masses may contain virulent bacilli is now well known. This is present day proof of the existence of tuberculosis, even though there is an absence of "ulcers" as small cavities and caseous masses were termed by Willis. The expression "ill formation of the lungs" (*mala pulmonis conformatione*) must not be understood as a malformation of the lungs, but rather as a diseased condition of the lungs.

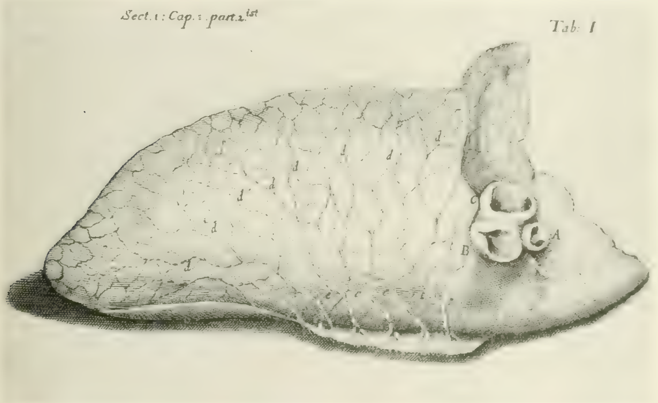

FIG. 3. AN ENTIRE LOBE OF THE LUNG SHOWING THE SUPERFICIAL LYMPHATICS

The manner by which the "consumptive matter" (infection) enters the lung is plainly stated when he says, "that anything that is an enemy (*inimicum*) to the lungs creeps in and is admitted chiefly by the trachea or by the pulmonary arteries, or perhaps by the nerves, but nothing by the veins or lymphatics, whose function is only to carry back or away the blood or lymph, and to bring in nothing at all (*atque nihil prorsus ingerere*)." Here Willis recognizes the two sources of pulmonary infection, the air passages and the blood stream (aerogenous and haematogenous infection). The nerves we will pass by, for they are no longer considered hollow tubes capable of conveying the animal spirits, a function quite necessary in the humoral pathology of Willis's time. Earlier in his discussion of the modes of infection, Willis discards the idea of "phlegm falling from the head into the lungs" as a cause of consumption.

Due to a long continued cough a "humor" may be deposited from the blood circulating through the lung in the lung substance itself. First of all, it enters the little tracheal bladders (*vesiculas tracheales*) which it distends and from which every morning it is removed by expectoration. This process is repeated from day to day, and so much of the humor gradually accumulates in the little bladders (see figure 2) that at last the sides of two or more of these litttle bladders give way and there is thus formed a reservoir (*lacum*), within which the consumptive matter accumulates and serves as a centre from which it is diffused through the lung, and the blood circulating in the lung becomes contaminated.

> The blood in the veins receiving the purulent matter in every circuit, it immediately delivers it into the arterial; from whence, since it cannot be fully excreted by sweat, or by urine, it is brought back by the pulmonary arteries to the lungs, where again being separated from the blood, it is everywhere conveyed into the little bladders of the trachea and into the lung passages; insomuch, that finally the whole frame of the lungs being filled, clefts or ulcers are formed as a result in many places, and all the other hollow spaces are filled with frothy ichor (*ichore spumoso*).

The sides of the ulcers or cavities thus formed frequently become callous (*callosos*), so that the matter contained in them does not enter the blood, but is expectorated in vast quantities. Although individuals thus affected expectorate large quantities of thick yellow matter every morning, Willis says they "frequently arrive to old age; insomuch some are said to have been consumptive thirty or forty years and to have prolonged the disease even unto the term of their life (*haud proinde abbreviatum.*) In the mean time others who cough or expectorate less, within a few months fall into a hectic fever, and in a short time are hurried into their grave." Here we have, on the one hand, a well drawn picture of chronic fibroid tuberculosis, on the other hand one of acute tuberculosis (*phthisis florida*).

After enumerating a number of causes of consumption which were connected with changes in the blood and "nervous juice," and formed part of the humoral pathology of his day, Willis describes causes which are associated with the lung itself. "1. A malformation of the frame of the breast. 2. An innate weakness of the lungs, or hereditary disposition to consumption. 3. Preceding diseases of the thorax, as a wound, a blow, a pleurisy, a peripneumonia, empyema, spitting of blood, the smallpox and measles. 4. The incongruity of the aïr inspired."

First: Malformation of the frame of the breast. After stating that it is necessary that the lungs have a free and unimpeded movement within the thorax so that they may be distended to their full extent and in this way be kept "whole and sound," Willis says:

> Wherefore, since the action of the lungs depends much on the frame of the thorax, as being the moving mechanism it must of necessity be, that by reason of its malformation, the function of breathing becomes defective in many things. There are two special kinds of malformations of the thorax, (namely, hunch-back, and wing-like scapulae) for which reason many are found prone to phthisis: the reason of which is, that in any such figure of the breast, being either depressed or made long, the lungs have neither so free and ample a space, nor can the muscles which move it be so strongly contracted as in a square breast.

The ancient authorities laid great stress on the conformation of the thorax and gave elaborate descriptions of the "phthisical chest," descriptions which even find their way into modern textbooks. Still, a malformation of the chest, especially a flat chest, is not a sure criterion that the individual is, or will be, tuberculous; when present it is more often the result of tuberculosis than a predisposing cause to tuberculosis.

Second: Hereditary disposition to consumption:

> When any one is found inclining to a consumption, he is questioned whether his parents were susceptible to the disease. Very many of these possessing a narrow breast and an elongated neck, and a very delicate constitution, contract a cough from the least occasion; neither can they endure a cold or moist air.

Some of these are unable to live in a city where the air is heavily charged with smoke, while others suffer no inconvenience. To all, however, a north wind is obnoxious and often leads to the development of some pulmonary disease.

It is interesting to note in this connection that Willis did not believe in the direct inheritance of consumption, but that there often existed an "innate debility" which, under certain conditions, permitted one individual to acquire tuberculosis more readily than another.

Third: "A phthisis is sometimes produced by, or is the consequence of, some previous disease." Among the diseases mentioned by Willis are empyema, pleurisy, pneumonia, abscess of the lung, and sometimes smallpox and measles. The inclusion of acute infectious diseases by Willis is very interesting in view of our experience following the epidemics which occurred in the various camps during the late war.

Fourth: The condition or temper of the air breathed in:

> Such is the influence of this on some consumptive persons, that the cause of the disease is sometimes wholly ascribed to the incongruity of the air wherein they live, and for a cure the alteration of air or soil is preferred to all other remedies. Therefore, many in our country who are troubled with a cough, or have a consumption, flock to the southern parts of France; and others in the meantime who cannot go beyond the sea, or will not, presently hasten to remove out of the smoke of the city into the country as a most undoubted refuge: wherefore all our villages near London, which enjoy a clear and open air, are esteemed as so many hospitals for consumptive persons. Nevertheless, all do not alike receive help from such a change of places; for many, either going to France or to country villages, do in those places rather find their graves than health. And therefore London is not presently to be forsaken by all phthisical persons: for I have known many subject (*obnoxios*) to a cough or consumption to have enjoyed their health much better in this smoky air than in the country. So that for cure of the same disease, while some avoid this city as Hades, others fly to it as to an Asylum.

Willis paid strict attention to his patients who suffered from a cough, and he describes three distinct stages or signs belonging to a cough:

1. When a cough arises ,whatever its cause, in a person predisposed to consumption it "will scarce ever be free from a suspicion of danger: but in a strong man, and one who has often before with impunity suffered from a cough it need not be immediately feared. . . . . If a slight fever with thirst and loss of appetite accompany this, there is hope that the blood being restored to its proper temperament, the cough will then cease of its own accord; but if it be long protracted, and does not easily yield to ordinary remedies, and produces much sputum, and that discolored, it must not be any longer neglected." This was excellent advice and can scarcely be improved by the modern clinician.

2. "But if to a cough daily growing worse with plentiful and thick sputum, a languishing and pining of the whole body, loss of appetite, difficult breathing, thirst, and fervent heat of the blood be added, there

is great cause of suspicion that it is come at least to the first limits of a phthisis (if not further)." This being the case Willis advises the use of remedies which will free the lungs from the "great quantity of matter" and at the same time remove the humors from the blood contained in the lung itself, or "transfer them to some other place than to the lungs."

3. "But if, beyond the state of the disease just described, plenty of sputum, and that discolored, shall be daily increased, and all other things growing worse, an entire loss of strength, and a hectic fever with a continual thirst, night sweats, an Hippocratical face, an utter loss of flesh almost to the dryness of a skeleton, happen upon all these, then for the most part no place is left for medicine, but only a sad prognosis; at least all hope of a cure being lost, we must insist upon anodynes, whereby an easy death may be procured."

It is interesting to find euthanasia advocated so decidedly back in the seventeenth century.

Willis is deservedly known in English medical history as a great reformer of pharmacology. In his day there was very little relationship between the disease and the means used for its cure. Antimony and other mineral poisons were freely administered. If one desires to learn the state of medical practice not only in France, but also in England, let him read the comedies of Molière. "The great dramatist had no use whatever for the medical profession, whose ridiculous side early excited his derision and against whom he seems to have cherished a lasting grudge, partly because of their inability to do anything for his own malady (consumption), and partly because he believed that they killed his only son and one of his bosom friends with their eternal antimony." (Garrison.)

Referring to the reckless manner in which the physicians of his day prescribed medicines and their penchant for new remedies, Willis says:

> they promise themselves presently to cure all diseases, and give them boldly in every case to the great injury, and not infrequently to the destruction of the patient; so securely and rashly are these executioners accustomed to trifle with human life, while they are led to the preparing or administering these medicines (in which always lurks some venomous sting) without any council or direction of method, but by mere chance and with a blind impetuosity.

Willis did not wholly succeed in establishing a direct relationship between the remedy and the disease being treated. As will be seen in some of the following prescriptions he made a sad failure. He must not, however, be too severely criticised for "Willis was the first to attempt the reformation of this degraded state of Materia Medica." (Berdoe.)

Not only are there many curious prescriptions included in Willis's treatment of consumption, but there is also much that is practical common sense. When a cough has been freshly acquired, he says it can often be cured by simple household remedies. In case these do not succeed, the patient should be placed on a low diet and carefully protected from the cold, by putting on heavier garments, by keeping in bed or in his room. Venesection is to be used rarely and only when the strength and constitution will bear it. Diaphoretics, diuretics and mild purges are often beneficial.

As examples of Willis's prescriptions, one for a mixture and one for pills have been selected; not because of their intrinsic worth, but because they illustrate the type of medicine frequently prescribed, and because they contain ingredients which he ought to have known were without effect:

> Take of the water of Snails, of Earth-worms, of each an ounce and a half: of the liquid Laudanum Tartarized, two drams: Syrup of Violets, an ounce. Dose, one spoonful at bed-time.
>
> Take of Millepedes or Hog-lice prepared, two drams: Powdered seeds of Nettles, of Burdock, of each half a dram: Oil of Nutmegs distilled, one scruple: Salt of Amber, half a dram: Juice of Liquorice q.s., form it into small pills; take three in the morning and three in the evening.

The following are much more agreeable and, no doubt, many present day patients (?) would not object to similar prescriptions:

> According to the constitution of the patient, sometimes simple milk, sometimes milk with wine, sometimes ale, or Brunswick Mum. . . . In a constitution less hot, especially if there be no excessive heat of the blood or Praecordium, to six or seven pints of milk, add one or two pints of Canary wine; and in a phlegmatic or old individual, instead of milk let the menstruum be ale or Brunswick beer.

The following, however, is much less attractive:

> In Winter-time when snails cannot easily or scarcely be procured, there may be substituted in their stead lamb's or sheep's lungs, also sometimes calves' lung, being half boiled and cut fine, with the ingredients already mentioned, and a suitable menstruum being added, let them be distilled in common Organs, or Rose-stills.

The preceding remedies are stated by Willis to be best adapted for the treatment of incipient consumption. The disease being fully established "the therapeutical indications are chiefly these three: viz., in the first place to stop the dissolution of the blood, which is the root of all this evil, and to make provision that it does not pour out the matter any longer in such abundance upon the lungs. Secondly, by expectorating the purulent matter accumulated within the lungs, and to clear it out quickly and adequately (*satis*). Thirdly, to strengthen and dry the lungs loosened from their unity (*unitatem*), or being too loose or moist or otherwise weakened (*imbecilles*), lest they daily become more impaired, and receive a greater amount of morbific matter."

Space will not permit of a more extended account of the remedies which Willis recommends. A detailed account of the treatment of a case of incipient tuberculosis, as given by Willis, shows that he did not always prescribe the drugs which have been enumerated, but that he had a very rational method of treatment of his own patients:

> It is now many years since I took care of a certain student, subject to a cough from his youth, and who was wont to frequently undergo the more painful affections of it, and those of long continuance. This person seemed of a melancholy temperament, of a sharp wit, of an indefatigable spirit, of a constitution inadequately strong, but because of the primary weakness of his lungs, did suffer when the blood dissolved into serosities. In Summer as long as he transpired freely, he enjoyed fair health; but in the Spring and Autumn, when the blood changed its temperament, those serous fluxes came upon him either of their own accord or from any slight occasion, and he fell easily into a cough with abundant and thick sputum; however, this condition frequently within six or seven days, as soon as the mass of blood (*cruoris*) was cleansed (*expurgatur*) by the lungs, gradually disappeared without any great use of remedies. But if to the above attacks of the disease some stronger causes were added, as chiefly the obstruction of the pores, and errors of diet, sometimes a more excessive and stubborn cough, neither immediately nor easily yielding to remedies and threatening nothing less than a phthisis did come upon him, then certainly the patient for the first days suffered slight shiverings in his whole body, and the sensation of a catarrh in his larynx; afterwards by frequent coughing with thin sputum, together with dizziness, he suffered from a sensation of numbness and a dropping at his nose (*narium stillicidio*).
>
> In this condition his best remedy was, and frequently tried with success, to drink a little more freely an excellent quality of wine, and other liquors very sparingly: in this manner the acidity and fluor of the blood being suppressed, and transpiration procured more freely, he was in a short time convalescent.

> Moreover, at night and early in the morning he was accustomed to take seven or eight drops of the tincture of sulphur in a spoonful of the syrup of violets, or of the juice of ground ivy.

At times this treatment and a well regulated diet did not bring relief, and

> the disease not being cured, extending over a long period and pressing him sharply for many weeks, at times for months, it reduced him to a remarkable thinness, and to the very brink of the grave. For the cough, increasing daily and being very troublesome, did very much impede and break his sleep, his strength languished, his appetite was lost, heat and thirst oppressed him; in the mean time his sputum increased daily and was expectorated in great quantity; . . . . moreover his breathing was difficult, his joints weak, and his flesh much reduced.

To relieve his thirst Willis allowed him to drink freely of an infusion, the principle ingredients of which were China root, sarsaparilla, and white and yellow sandalwood.

> In the midst of this course of treatment, although he had a weak pulse and a subnormal temperature (*temperamento frigidore*) we breathed a vein in his arm. But, with these remedies, he derived the greatest help from the open air (*ab aere aprico*), which for the most part he daily enjoyed, either by riding on horse-back or in a coach; for from this time he first began to recover his appetite, his digestion, and his sleep; following this there was a gradual relaxation of his other symptoms, till at length he recovered his entire health. Since then as often as he was afflicted with a stubborn and tedious cough, he made use of a similar method and with like success; and now, although he lives quite exempt from the disease, he is careful to avoid all occasions whereby either the pores might be shut, or the flux of blood or its precipitation into serosities might be provoked.

It would be exceedingly interesting to give in detail Willis's *Praefatio* to the second part of his *Pharmaceutice Rationalis*, for it shows so clearly the spirit which actuated him in his studies. He realized that what he considered necessary to be done "is more than the task of one man or generation;" and, although three centuries have passed, many of the things he desired to do still remain unfinished.

Three characteristics deserve special mention in connection with Willis's work on Phthisis:

1. He studied both the macroscopic and the microscopic structure of the lung. As the result of these studies he gave a description of the lung which was superior to any preceding description.

2. He made numerous autopsies and endeavored by combining his clinical with his postmortem observations to obtain a better knowledge of the pathology of the disease, anticipating Morgagni by nearly a century.

3. He observed carefully the effect of the remedies used and formulated a method of treatment which anticipated the modern "open air" treatment of incipient tuberculosis.

In concluding I can give no better estimate of Willis, the man, than that given by Hirsch, who says, "As an anatomist, physiologist, and practising physician, and at the same time celebrated man, Thomas Willis occupies the first rank."

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BREHMER AND DETTWEILER

A REVIEW OF THEIR METHODS OF TREATMENT OF PULMONARY TUBERCULOSIS

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The three pioneers in the modern treatment of pulmonary tuberculosis were Brehmer, Dettweiler, and Trudeau. They all used rest and exercise as essential factors in treatment, although their views with regard to these did not agree. It is necessary to examine the methods and the development of treatment of each of these men in order to fully understand the modern treatment of this disease. Inasmuch as Brehmer was the first great figure in the modern method of treatment, I shall deal with him first.

HERMANN BREHMER

Hermann Brehmer was born in 1826 and began his active career in 1854. It was due to his dominant personality and energetic will that we now see such brilliant results of his work. He had many difficulties to overcome, and his whole life was a constant struggle to convince the medical profession that tuberculosis is a curable disease and that his methods were sound.

When he began to practise, the view was firmly established everywhere that a person who showed evidence of pulmonary tuberculosis was doomed to death. We must also remember that medical methods of investigation were then not nearly so accurate as they are to-day, so that the physician was often not much earlier in making a diagnosis of phthisis than the patient himself and his friends. Pulmonary hemorrhages, marked emaciation and hectic appearance were usually the first symptoms for which the patient consulted the physician, and as a rule he was then, even in the most favorable cases, in the second, often in the third stage of the disease.

As a result of Rokitansky's findings that ninety per cent of those who had not died of tuberculosis had healed tuberculous lesions within the normal lung tissue, Brehmer started to investigate the causes of these spontaneous cures. He concluded that it would be possible to get healing of tubercle in the form of scar formation, calcification, and adhesions, before disintegration and destruction of lung tissue with their accompanying harmful effects on the whole body had set in. He believed that the disproportionately large size of the phthisical lung as well as the small heart of the consumptive and, as a result, the deficient circulation of blood in the human lung comprised the cause of pulmonary tuberculosis.

In 1853 in his inaugural address he made the statement, "Pulmonary tuberculosis is curable." This was received with much scepticism and he met with much opposition from many physicians on account of his new teaching. In spite of this a Hannoverian practising physician, convinced of the truth of Brehmer's theories, sent him patients.

As he was young and had only limited means, the opportunity was not given him to test his theory of the curability of pulmonary tuberculosis in practice and to make an estimate of it on a large amount of clinical material. Accident, however, led him, a son of Silesia, into the idyllic mountain valley of Görbersdorf, which at that time was entirely unknown. Görbersdorf is a little village in what was then the Prussian province of Silesia, Germany, and is situated in a mountain valley 1715 feet above sea level.

In 1849 Marie von Colomb, the eldest sister of Brehmer's first wife, established a small hydropathic institution in Görbersdorf. For a time this was supported by Brehmer. When, however, he found that it could not exist as such, he took it over and began his life-work to demonstrate his theories. The beginning was very hard. He began with a few patients, with one cow to furnish milk for them, and a lean horse to fetch coal from a distant place and patients from the station. The establishment consisted of a modest little cottage. For some time he had great trouble to keep the sheriff from taking his cow and horse, so hard was it for him to make both ends meet. After a few years, however, his great work became known, and physicians and patients flocked to Görbersdorf to be taught and treated by him.

A new problem now developed. He planned to make Görbersdorf a world health resort, but found almost insurmountable obstacles in the petty spirit of the natives of the village where he had distributed his patients in private houses. He, therefore, decided to build a *Kurhaus* with forty rooms. This would also contain entertainment rooms and kitchens. At this time this was an unheard of and luxurious undertaking. He raised the money with great difficulty. When the structure of the present old *Kurhaus* had reached the first floor, heavy rains set in and the entire building collapsed. He began again to build it and in 1862 the *Alte Kurhaus* was finally finished. In the course of time more buildings were added and in the early eighties a new *Kurhaus* for an additional sixty beds was built.

In a certain sense Brehmer was a pupil of Preissnitz, whose methods of treatment he had learned while a student during a holiday visit at Grafenberg. He, therefore, included hydrotherapy as a large factor in his plan of treatment and devised the forest douche (*Walddusche*). For this the patient had to ascend each morning to the *Walddusche*. He was then douched with a very strong stream of water which fell from the height of five metres and which was of the thickness of the thumb. This lasted up to thirty seconds and the water was ice cold. The patient was then rubbed dry. To-day no physician would dare to offer his patients such heroic treatment, but Brehmer superintended the douche himself and overcame all the objections of the patients to using ice cold water. In his *Therapie der Lungenschwindsucht* he wrote:

> The water of the douches must be cold and fall with considerable force. The stream must form an even, homogeneous column which should have the same diameter above and below. The majority of douches do not meet this requirement; patients have previously been subjected to merely a sprinkling, but not to a powerful douche. With most douches the water pipes are so tortuous that the force of the water is almost exhausted before the water strikes its object. The size of the openings for the spray is also not such as to secure equally favorable results. The douche is also of particular value for pleuritic exudates, which are very quickly absorbed under its influence. It is, however, a dangerous remedy and should be administered only by the physician.

In addition to this hydrotherapeutic building, he put up an observatory for meteorological observations, since wind, humidity and temperature and barometric changes exerted, according to his view, far reaching influences on the condition of the pulmonary invalid. He fitted out the observatory with expensive pieces of apparatus and this part of his work gave him great enjoyment, as he had been a natural scientist and mathematician before he began to study medicine.

He also had a large laboratory which trained a large number of physicians, who afterwards became famous; for instance, Petri, Cornet, Kobert, Czaplewski, Möller, Köhler, Cibulski, and others. Flügge said, "Hardly in any other scientific institution where work is done have Koch's experiments been repeated so extensively and with such thoroughness as in the institution at Gorbersdorf."

Upon the discovery of the tubercle bacillus it was immediately clear to Brehmer that this could be of far reaching significance to his entire undertaking. For, after Koch's discovery became more widely known, a vigorous agitation set in against Görbersdorf, against Brehmer and his views, and chiefly against the institutional treatment of tuberculosis. Since the contagious character of the disease was established, it was believed that cure was impossible in an institution, on account of the constantly recurring infection with tubercle bacilli. Bacteriology completed Brehmer's views. Now, no disproportion of heart and lung leads to tuberculosis because of poor nutrition of the lungs, but besides disposition a pathogenic agent is necessary, namely, the tubercle bacillus. In order to meet the opposition to sanatoria he established a very perfect system of disinfection and thus overcame this antagonism.

Brehmer is preëminently known by his treatment of pulmonary tuberculosis in closed institutions. He was the originator of institutional therapy, although sanatorium treatment now differs in many respects from the original method. Treatment and observation of pulmonary patients in a sanatorium built for this purpose, which admits only lung patients, situated in a suitable climate, with abundant nourishment, fresh air treatment and hydrotherapy,—these were the basic principles of Brehmer's therapy, which are still of value to a very large degree.

Dettweiler, who was at first a patient and later an assistant of Brehmer, established a sanatorium at Falkenstein, and, soon after he began his work there, differences of opinion between him and Brehmer arose. He did not accept Brehmer's theory of "too small a heart." He considered that Brehmer did not place sufficient value upon the regimen of the institution, which, according to Dettweiler, together with education in healthy habits of living, formed the most important factor in treatment. In answer, Brehmer said, "They have learned in the institution how to live and what to avoid." The local conditions at Görbersdorf were against strict regimen. At the height of the season the place was overcrowded with patients undergoing treatment, and control of them was impossible. In addition there was no rest cure (*Liegekur*) and thus no daily meeting between physician and patient. There was also no compulsion to see the physician and thus it was impossible for the latter to be responsible for the patient's behavior. Medical treatment was not included with the board, but the physician sent in his account at the end of the patient's cure. According to Dettweiler, Brehmer did not hold regular office hours until the last few years of his life. Up to that time, he could only be seen professionally at the douche hours, which he personally supervised until he died. In his time, the relation between physician and patient was such that the latter could call upon the former at any time, but he was not forced to act according to the physician's advice.

There were other serious differences of opinion between Brehmer and other physicians, especially Dettweiler, because Brehmer believed that there were localities which were "immune" against tuberculosis, and that only such localities were suitable for the treatment of this disease. Dettweiler's view was opposed to this. According to him it did not matter where one treated tuberculous patients. What mattered was how it was done.

Brehmer's advocacy of abundant feeding is to-day still a factor in treatment, although we no longer go to such extremes. His use of strong wine, especially of Hungarian wine and of cognac, was much less than was usual at that time in the treatment of tuberculosis.

He introduced the open air treatment but did not favor *Liegehallen*. He called them overcrowded rooms without the fourth wall. Dettweiler introduced the *Liegekur* (cure in a reclining chair). The *Liegehalle*, however, possesses the great advantage that even the most thoughtless patient is obliged to take the cure. For many patients, also, it is easier to take the cure in company. The absence of *Liegehalle* at Görbersdorf was a drawback. The absence of the *Liegekur* (rest cure) in his time at Görbersdorf permitted many patients with fever to walk around in the open air. According to our present views, this did much harm.

If Brehmer's treatment of fever cases was not complete, he was nevertheless the first to demand and carry out a regular two hour measurement of temperature. He was very accurate in his temperature observations and had rectal or axillary temperatures taken, not mouth temperature, and a two hour temperature recorded, at first during rest in bed. In his time, however, the clinical therometer was much more cumbersome than it is to-day and a rectal temperature was necessary for accuracy.

The first edition of his work was published in 1857 (*Die chronische Lungenschwindsucht und Tuberkulose der Lunge*, Th. Chr. Fr. Enslin, Berlin) and was completely ignored by the medical journals. The

Wiener medizinische Wochenschrift was the only medical publication that reviewed it and its criticism was unfavorable. In 1869 he published the second edition with the same title and by the same publisher. His principles of treatment by this time had become more fixed, and the results were now very numerous and exceedingly favorable.

He took as a basis for his treatment the assumption that tuberculosis is caused by a relatively small heart, an insufficient blood supply to the lungs, and a lack of nutrition to the whole body. At this time (1869) his treatment was as follows: He considered it to be essential that treatment should have as its aim good nourishing food. Inasmuch as man is neither carnivorous nor herbivorous, the diet should be a mixed one with plenty of vegetables. He claimed that it has not been proved that eating increases fever. In his sanatorium, patients had from five to seven meals in twenty-four hours. Frequent meals of moderate quantity were considered better for delicate stomachs than less frequent large meals.

Wine was an important article of diet and Hungarian wine was preferred above all others, because of its high percentage of phosphates of lime and magnesium. Through its alcoholic content, it was thought to lessen the wasting of the consumptive, and through its phosphate of lime assist in building up tissue. The usefulness of wine was not limited to its value in diet. It was used to combat the chills of hectic fever and to moderate the resulting high fever. Cognac was also used for night sweats. Brehmer gave such patients two teaspoonfuls of cognac to a glass of milk on retiring and the results were excellent.

Of equal importance with the strong nourishing diet was the use of fresh air which was so very much neglected and which cannot be recommended too strongly. Without this the best diet may produce no result. The patient should be constantly in the open air. This has been practically the only reason why patients are sent to Southern health resorts. Already, at this time in England, Cormac allowed his patients to sleep with open windows, not only in summer but also in winter. It was only prejudice which made patients think that night air was harmful. It is of importance to emphasize this fact which Brehmer insisted upon at this time, namely, that night air is not harmful.

Another factor, which he added to nourishing diet and fresh air, was increased activity of the skin. For this purpose he had employed damp rubs since 1854. These produced not only increased activity of the skin but also an increased physiological frequency of the pulse. Rain baths were also used, either alone or followed by a stream douche (*Strahlendusche*). The rain bath (*Regenbad*) was a douche so adjusted that the water fell on the patient as rain. With regard to its danger, Brehmer said that there is no more senseless fear than that it can cause hemorrhage. In the almost one hundred thousand douches he had given until then, he had never seen hemorrhage as a result, although he had often seen brilliant effects from its use in cases which were spitting blood. It is a remedy which should not be left to the hands of an assistant (*Diener*), but should be directed by the physician himself. The duration varies from five to forty-five seconds and is determined by the condition of the patient. They should, therefore, be instructed to communicate any change in their condition before they take the douche.

Immediately after the rain bath, the skin is more active and the patient feels very much better. Its most striking action is seen as a specific remedy for hectic fever. If given at the right time, at the onset of the chill, it will retard it and shorten its duration, and within a short time entirely do away with it.

Although he considered the rain baths as an excellent remedy for pulmonary tuberculosis in general, yet they are not necessary in many cases. The *Strahlendusche*, when used for caseous infiltration of the lungs, favors absorption of this in a remarkable degree in many cases, and thus cures. It cannot be used in all cases and is absolutely contraindicated in all cases in which, immediately after its use, there is no reaction and no feeling of warmth, and where the patient is unable to produce the necessary amount of warmth in order to replace its loss.

He found that those patients, who continued the use of rain baths at home during the winter, got through the winter very much better than those who did either nothing for the activity of the skin or else only used rubs.

With regard to the douche, it should be observed that it can only act if the water falls with a certain strength or pressure and if the stream remains completely concentrated until it reaches the ground. All douches, of which the water falls free and the streams are dispersed, are ineffectual, even if the source be ever so high above the douche room.

With liberal diet, fresh air, suitable exercise in the open air, mental rest and baths which are supervised in order to produce a greater activity of the skin, we will get a result in many cases in the treatment of phthisis which are not too far advanced.

With the above method of treatment, it cannot be said that every patient is cured. Improvement and cure are not identical. Cure can only result if the condition of the patient is suitable for it and if he will give the necessary time to it. The latter usually does not occur, as the majority are satisfied with improvement. To these requirements for cure Brehmer adds another which he considers as essential, namely, the lessened air pressure which is obtained from mountain air.

He considered it to be essential for patients to be in the open air as much as possible, so as to enjoy the fresh air, whether they take this in the form of walking exercise or driving. They should be sent only to those mountain valleys which are free from pulmonary tuberculosis and sheltered from winds and surrounded as much as possible on all sides by mountains. Görbersdorf possessed all these advantages.

Until the year 1869, Brehmer had treated 958 patients in his sanatorium and 315 of these were in the stage of "colloquation." Only 47, or 4.8 per cent, of these died at Görbersdorf. On the other hand, 20 per cent were permanently cured, in spite of an average duration of sanatorium treatment of only eighty-six days.

With regard to the duration of treatment, he said that this should be continued until the disease was cured. This will depend upon the grade of the disease and upon the general constitution of the patient. A recent case can be treated much more easily than a chronic one. The sicker the patients, the more unfavorable they are.

What to do with the patients during the winter was the problem now (1869) presenting itself. At first no one thought that they could remain in the mountain valley during the winter months. It was assumed by everybody that they would be cut off from all social intercourse in winter and would have to keep to their rooms throughout the entire day, and thus would not take the air cure. It was found, however, that the winter weather in the mountains was capable of allowing patients to take their exercise with great regularity. They were unable to get any mountain climbing on account of the deep snow, but the other curative agencies offset this disadvantage. It was considered absolutely necessary for these patients to get their rain baths throughout the winter, but in a well heated room. At this time Brehmer was also building glass enclosed verandas so that the patients could take their walks.

An important point with regard to exercise is cited by Brehmer, namely, that Bennett of Mentone was already warning his patients against too much exercise and the danger of walking themselves to death. It is thus seen that doubts were already beginning to arise as to whether exercise was not being pushed to too extreme a degree.

In order fully to understand Brehmer's treatment at this time (1869), I may give some of his case reports:

Case II. (page 322, second edition) Male, twenty years of age, two years previously had had a hemorrhage. Percussion full and clear throughout. Auscultation, right front to third rib, weaker vesicular breathing than on left, and prolonged expiratory sound. Sputum sparse and slimy. Treatment, much exercise in the open air, rubs, later rain baths, the *Strahlendusche* on the right side of the thorax. The patient remained a little less than five months and then had no physical signs. Eight years later he was in excellent health.

Case III. (page 324) Male twenty years of age, sick for three or four years. Physical examination showed a light and full percussion tone, but weaker than normal, and on auscultation there was heard indefimite vesicular breathing with prolonged expiration on the left to the third rib and on the right in the supraclavicular fossa. Treatment: moderate exercise, mountain climbing, rain baths of thirty seconds. The patient was cured at the end of four months, and remained well and later entered military service.

Case IX. Male, aged thirty-six years, hemoptyses in 1855 and 1860. On examination he had slight cough and little expectoration. Percussion was normal both front and back on the right side; on the left side in front it was duller and fuller to the second rib than on the right and the same behind in the supraspinous fossa. Auscultation, vesicular on the right both in front and behind; on the left, in the supraclavicular region and supraspinous fossa, weak, bronchial and indefinite to the second rib; from there downwards, however, vesicular breathing. Treatment: the usual exercise, Rhine wine, and a rain bath of sixty seconds' duration. The patient was cured at the end of two months and has remained well for seven years.

Case X. Male, thirty-three years of age, very emaciated. Entered the sanatorium in May, 1859. He had repeated hemorrhages from 1857 to 1859. Examination: short cough, sputum slimy and purulent, quantity about one tablespoonful. Percussion: on the left side over the entire front there was a light, and in some places particularly over the upper part, a distinctly tympanitic sound. On the right side in front down to the third rib there was a dull sound and from there downwards a full and clear sound. On auscultation there was heard cavernous breathing over the entire left side, and over the upper part of the left side large consonating râles; on the right side there was heard bronchial breathing to the third rib and from there downwards weak vesicular breathing. Treatment: the patient remained four months. Treatment was as usual. In spite of the tendency to hemorrhages, mountain climbing was not forbidden him, but as soon as his strength allowed it, this was ordered. In the winter of 1859–1860 he had a slight hemoptysis. In the winter of 1860–1861 he was able to take long walks, even for several hours at a time. He died several years later as a result of dissipation.

Case XI. Male, age fifty-two years, hemorrhage in 1851 following "grippe." This was followed by cough and copious purulent expectoration. In 1855 he had pains in the kidney region with catarrh of the bladder and occasionally blood in the urine. In 1859 he again had pulmonary hemorrhages. In June 1869 his condition was as follows: A powerfully built but emaciated man whose whole impression was bad. "The thorax is paralytic; above and below the right clavicle there are deep depressions; the intercostal spaces are wide; inspiration superficial; and under the right nipple pain on deep inspiration; respirations twenty-four." Percussion, normal over the entire front and back of the left chest. On the right side there was an empty and light sound down to the second rib in front, and likewise behind in the supraspinous fossa. Auscultation was vesicular over the whole left side; on the right side in front over the supra and infraclavicular region there was bronchial breathing, weak bronchophony, and loud, small, bubbling, consonating râles. These were also present in the supraspinous fossa. There was also indefinite breathing to the third rib and vesicular breathing from there down. Treatment was almost the same as with the other patients, except that more exercise was ordered in the fir forest. Within a short time he was able to ascend the Reichmacher twice daily without getting tired. In all, he took about six to seven hours' walking exercise in all kinds of weather. In two months his expectoration had almost entirely disappeared. He remained in the sanatorium for three months. A dry cough was the only symptom of disease which remained. This also disappeared within four months by the continued use of the rain bath. He has remained well for eight years.

Note—The Reichmacher is a mountain one thousand feet higher than Görbersdorf. Healthy people make the ascent in half an hour. It is this mountain which Brehmer's patients had to ascend in order to receive the *Strahlendusche* from him.

These case reports are sufficient to give us a good idea of the class of cases which Brehmer was treating at this time and the kind of treatment employed.

In 1889 Brehmer published the second edition of his book *Die Therapie der chronischen Lungenschwindsucht* (published by J. F. Bergmann, Wiesbaden). It is of importance to examine his methods as described at this time.

When he began his work and made the assertion that pulmonary tuberculosis is curable, he was laughed at and called a charlatan. By

1889 every clinical professor taught the curability of phthisis, at least theoretically.

To bring about cure, he considered that certain conditions are necessary, and the first integral condition of his method of treatment is the closed sanatorium, that is, the closed sanatorium which takes only tuberculous patients, so that other diseases are treated only when these patients are suffering from them or develop them later.

A further cardinal point in his method of treatment consisted in the proper selection of a place for the sanatorium. He assumed that in phthisis it was necessary to lessen the disproportion between heart and lung function, either by increasing the substance of the heart or increasing its driving power. Therefore, every sanatorium for pulmonary tuberculosis should be in the mountains, because the diminished pressure of mountain air exercises this influence, since it increases the frequency of the heart beat physiologically, and strengthens and enlarges the heart muscle through this regular, increased contraction. The heart muscle is further strengthened because it assimilates more nourishing material, for it is an almost uniform effect of life in the mountains that the appetite is usually immediately increased.

Generally speaking, it cannot be determined to what degree the air pressure must be lessened, that is, how high the locality must be situated in order to obtain the desired result. No mistake will be made if we say that the air pressure must be so lessened that under its influence, in association with other climatic factors, the inhabitants who were born in the locality are free from tuberculosis, that is, that the place must be "immune" to the disease.

Dettweiler opposed Brehmer's view that there are places that are immune to tuberculosis (Dettweiler, *Behandlung der Lungenschwindsucht*, 1884, p. 23). He said that there are no specific properties of air which we have to thank for their favorable action on tuberculosis, but that the use of pure, fresh, and not too warm, air is a chief curative measure. To-day we know that Dettweiler's view was the correct one and that there are no places immune to tuberculosis.

It is interesting to see what great importance Brehmer came to place upon supervised exercise. In the earlier treatment, which I have described, he advised mountain climbing in rather an indefinite way. The exercise was not strictly supervised. He now (1889) says that perhaps the most important factors in the treatment of pulmonary tuberculosis are the walks and grounds of a sanatorium.

We wish to strengthen the heart muscle, even to increase its amount. The muscular substance is increased by exercise. We must therefore exercise the heart muscle, and this exercise is best carried out by walking exercise. Moderate physical exercise increases heart action and prevents accumulation of fat. At the same time we must always remember that we are dealing with a weak, not normal heart. Care must be taken that the heart is not fatigued by the physical exercise, for every tiring of the muscle means harm to it.

I wish particularly to emphasise the following views which Brehmer had with regard to exercise: It will be seen that he is now much more careful of his supervision than in 1869. He now states that every form of fatigue is harmful to the tuberculous patient and that every form of fatigue of the heart is poison to him. The promenades for consumptives must be so arranged that patients cannot become tired and that thereby every fatigue to the heart and overstrain of the lung is excluded. For the first purpose there must be paths with different but never abrupt ascents. For the latter purpose the opportunity must be offered to patients to rest themselves at any time, before they observe any kind of tax or discomfort, whether these be from heart or lung. There must be many benches on the promenade walks, on which the patients can rest themselves. The institution must provide these measures. Their use is for the patient, on whose judgment and by whose correct employment so much of the success of the treatment depends.

He then refers to the fact that the literature advises that the physician should prescribe and supervise the amount of exercise. He says that the physician does not do it, because he is quite unable to visit his patients before breakfast in order to give them their directions. He would have to visit the first one very early and disturb his sleep. According to his view it would also be incorrect for the following reasons: Everybody is different to-day from what he was yesterday; what is easy for him to-day may be harder for him to-morrow. This occurs to a higher degree with sick people. *Exercise must be in accordance with the strength of the patient and the condition of the disease at the time.* This is most important, in order to strengthen the heart gradually by exercise, with avoidance of every fatigue, and to guard the lungs from every overexertion. Only the patient himself can determine the amount of this exercise, for he learns to watch himself every minute, so as not to tire himself or even to tax himself.

His instructions to the patient from the day of his arrival were as follows: That he should be as much as possible in the open air, particularly in the forest or in its neighborhood, wherever his wishes led him; that he should therefore take walking exercise, and that this exercise at first should be on level paths; that he must regulate this himself; that he must never tire himself and never put the lungs to forced activity; that in the evening when he goes to bed he should not be aware of the fact that he has walked. The task to take plenty of exercise and never to become tired is solved by his never placing behind him a large extent of country, but always to become thoroughly rested before he observes any kind of fatigue. The patient must do exactly the opposite to the healthy man who rests when he becomes tired, for the lung patient must rest although he is not tired. He merely sits down, because he is ordered, so that he cannot get tired. Brehmer also instructed every patient that he must always walk without having a fixed goal, because of the danger of exceeding his strength and thereby tiring himself. He also told the patients that they must remain exclusively on the grounds of the sanatorium while on their walks, because it was only there that they would find smooth artificial paths with slight ascent and continuous benches even up the mountains, where they could rest themselves at any time. In addition, he made the patients pay attention that they should never walk rapidly, because fast walking causes shortness of breath through violent heart action, and taxes the lungs. The patient must go slowly, must keep mouth closed, and quietly inhale and exhale through the nose.

Under no condition should he breathe so deeply, in order to introduce as much pure air as possible into the diseased lung, that he thus practises lung gymnastics. Volland in Davos-Dorfli has directed attention for a long time to the harmfulness of these lung gymnastics, and Liebermeister has recently done the same thing. The lung is the diseased organ which should not be taxed, at least not more than is necessary for physiological purposes. Inasmuch, then, as every exercise reacts on breathing, many benches were placed on all the walks, even on the so called "level paths", and resting places were thus made, so that the patient could rest himself whenever he wished. "Level paths" is a very relative term if one does not specify the conditions of ascent. The promenade walks made on the grounds, even on the mountains, are relatively level paths, which even in their greatest ascent are not steeper than some paths in health resorts for lung patients from the principal street to the rest houses. For example, a path to a point which lies one hundred and twenty feet higher than the institution is about thirty-two hundred feet long; the gradient is therefore 1 to 27. This path is upgrade and yet it is perhaps less steep than the level paths in the Swiss health resorts. We therefore see that mountain climbing on Brehmer's regulated paths and mountain climbing in Switzerland are two very different things. Real mountain climbing on the usual mountain paths should never be undertaken without medical permission. Very many patients left Görbersdorf with a good result without ever having ascended a mountain in this sense.

The arrangements of the institution should provide that the patient may rest as soon as he wishes. It can be ascribed to this that of about fourteen thousand tuberculous patients Brehmer could point to only one case which was harmed by overexertion. This case was a physician who had pulmonary tuberculosis and who wished to make a mountain excursion by wagon. Brehmer warned him that the path was bad and that he would have to return on foot. A thunder storm was also threatening. This was all to no purpose. The patient made the trip, reached the top of the mountain, and as the thunderstorm was still threatening he began rapidly to retrace his steps. A severe hemorrhage set in almost in front of his dwelling, and he died in three days.

Brehmer believed that no path for walking should lead down hill. There is always the possibility thatt he patient will use such a path, and therefore the constant danger that he will go too far, and thus overtax himself on his return. An institution should therefore be at the lowest point of a valley and not on the slope of a mountain, so that all walks, except the level ones, should gently run up hill. Benches should be placed at regular intervals along the paths and these should constantly remind the patient to sit down. At Brehmer's institution benches were placed at twenty paces apart along the paths, which were about seven kilometres long and led to the summit of a mountain which had a distant view. These paths were always on the grounds of the sanatorium. Along the promenades were little pavilions where patients might find shelter in bad weather and where they might rest. In this way it was possible for patients to exercise even in bad weather, and they were allowed to go out in almost all kinds of weather except when there were heavy winds.

Since my object is to examine his method of using rest and exercise, I shall not describe Brehmer's method of treating fever. He found, however, that bed rest alone frequently overcame chills and fever. He mentions having kept one patient in bed for seven months on account of fever. This is interesting, because we see that he used complete bed rest treatment with fever cases, although he does not indicate that he used rest treatment for afebrile cases. Up to this time, however, he had not grasped the full value of rest treatment. For instance, in his treatment of chills and fever he mentions that the chill occurs in many cases after the patient gets up and dresses. In these cases it was most important to keep the patient in bed for at least an hour longer than the chill lasted the previous day. It was then important for the patient to drink a glass of hot grog or wine, one-half hour before he got up. Frequently, through bed rest alone, it was possible to avoid the chill; but also frequently not. From the above it is clearly seen that his rest treatment for chills and fever was very imperfect. He did not continue bed rest treatment long enough with fever cases, but would let these get up too soon.

An examination of Brehmer's treatment shows that no particular emphasis is placed on rest treatment. He did not employ it in a thorough manner with his fever cases, although it was used on these to a moderate extent. His method of using exercise treatment became very much modified from 1869 to 1889. In 1869 mountain climbing was advised as a routine treatment, as is seen in some of the case reports which I have given. In 1889 we see that he used extreme care with exercise. All this shows the influence which Dettweiler, with his reclining treatment, was having on Brehmer. The latter evidently did not wish to acknowledge this, but his writings clearly show it.

To-day we know that Brehmer was not correct in some of his hypotheses. For instance, we know that there are no "immune" places, that is, places which are immune to tuberculosis. We also know that the cure of tuberculosis is not confined to mountain districts, but that the disease can be successfully treated in any climate. We also know that the small weak heart and the relatively large lung are not the causes of pulmonary tuberculosis. At the same time he stands out as *the great figure* in the modern treatment of this disease. He is the father of the modern method of treatment. Dettweiler and Trudeau and the other pioneers in tuberculosis work got their inspiration from him. Brehmer cured a great many patients of their pulmonary disease, and to accomplish this his method of treatment had enormous value. I think we have improved upon his methods, but it is a question whether any of us will have as many cures to our credit as he had. He died in December, 1889, at the age of sixty-three.

PETER DETTWEILER

Peter Dettweiler was born August 4, 1837, in Wintersheim near Worms and was the son of a tenant farmer. His first pulmonary hemorrhage occurred while he was a student, and he then entered upon long years of illness. Finally, however, he became cured of his pulmonary tuberculosis and then paid very little attention to it. He was a field physician during the wars of 1864, 1866 and 1870.

His pulmonary disease sent him to Brehmer at Görbersdorf. He was first a patient and later an assistant of Brehmer, and at this time his observations on both himself and others convinced him that pulmonary tuberculosis was actually curable. This idea took possession of his enthusiastic nature and ruled his entire life.

As his ideas ripened they gradually became opposed to Brehmer's. This led to differences of opinion and the two men finally separated. Dettweiler's high opinion of Brehmer, however, was not confined to himself, but was passed on to his own pupils.

Rest cure in the open air must be considered Dettweiller's greatest service. He also constantly asserted that climate and elevation play no essential rôle in the treatment of pulmonary tuberculosis. These views helped to vulgarize tuberculosis treatment and made possible the establishment of sanatoria for less wealthy classes of people. Dettweiler himself translated theory into practice when he established the first German people's sanatorium. This was first started at Falkenstein, in addition to the institution which was already there for the well-to-do. It was soon, however, removed to Ruppertshain in the Taunus mountains.

Dettweiler got his greatest experience at the institution for the wealthy at Falkenstein, which also owed its prosperous existence to him. While he was director of the institution, from 1876 to 1895, the reputation of the sanatorium became world-wide. In 1895 he retired from its administration and became a consulting physician. From his cottage in Cronberg in the Taunus mountains he carefully observed not only the doings of the institution at Falkenstein but the whole antituberculosis movement. Chiefly interested in the multiplication of people's sanatoria, it was a great satisfaction to him to see his own practical example followed to such a large degree everywhere.

He died on January 12, 1904, in Cronberg at the age of sixty-seven years. The cause of his death was paralysis of the heart (*Herzlahmung*) and was very unexpected. (*Geheimrat Dr. Peter Dettweiler, Münch. med. Wchnschr., No. 6, February 9, 1904, Dr. Bezold, Falkenstein.*)

Rarely has a valuable measure been so quickly accepted by the medical profession, and with so little opposition, as the rest treatment, and particularly the open air-rest treatment in pulmonary tuberculosis. The cause of this lies in its simplicity. Although we owe to Brehmer the first elements of the present day treatment of phthisis, it is quite remarkable that he never grasped the great significance of the open air-rest cure. Even up to the time of his death he was unable to accept it.

Dettweiler was a patient at the sanatorium at Görbersdorf during the summer months of 1868 and 1869, and was second physician in the institution from March, 1870, to August, 1875, with an intermission of seven months due to the Franco-Prussian war. At this time the use of fresh air by the patients was limited to their walks, and to the abundant opportunities to sit in the park and forest. Both depended upon the strength of the patient and the atmospheric conditions which prevailed at the time, and which are just as changeable in the mountains of Silesia as in the other mountainous districts of Germany. As a consequence, patients were compelled to remain in their rooms for a greater part of the time, particularly in the unfavorable seasons of the year. These rooms, moreover, were not altogether suitable. Partly on the advice of Dettweiler, but stimulated particularly by the treatment which was being so successfully carried out at Davos during the winter, Brehmer determined to erect new buildings, so as to correct these unfavorable conditions as much as possible. Comfortable, hygienic and relatively favorable rooms were obtained, and, for the time, the new buildings were almost luxurious. Only the more vigorous patients, however, were able to brave the frequent changes of weather and take systematic walking and mountain climbing exercises. Very many patients became hardened by them. Dettweiler asserts, however, that others were harmed by the forced exertions and the frequent inability to sit down and rest when they wished to do so (*Einige Bemerkungen zur Ruhe-und Luftliegekur bei Schwindsuchtigen, P. Dettweiler, Zeitschr. f. Tuberk., 1900, i, 96*). Brehmer, however, states that of about fourteen thousand tuberculosis patients he could point to only one case which was harmed by overexertion of the heart, and that this patient suffered harm and afterwards died as a result of disobeying orders.

While Dettweiler was in Brehmer's institution he was suffering from pulmonary tuberculosis and had abundant opportunity to observe a great many patients. He soon concluded that "the consumptive is a physical and usually a nervous weakling, and needs much more rest than one ordinarily takes." Proceeding from this viewpoint he began to use the hammock in the summer of 1868. In the war of 1864 he had used it with great benefit. Hammocks were soon used during the good summer months by numerous other German health resorts.

Brehmer and Dettweiler, however, did not at this time think of a continuous open air-rest treatment during the late months of the year. It still needed many experiences and a slow ripening of his judgment in the first years of his management at Falkenstein, before Dettweiler had the courage, at the end of 1879 and the beginning of 1880, to make his first serious attempts at a real permanent open air treatment, even in the so called bad seasons of the year (late autumn, winter and early spring). He began with some very sick patients whose continued confinement to bed in their rooms seemed to be very painful and unsuitable, and he hoped to influence the fever favorably by means of cold air. These patients were preferably intelligent and tractable women, and they encouraged him to carry out the experiment during the first winter.

At first beds were used from the patients' own rooms. However, as soon as the beneficial results of the new procedure were evident in the great majority of cases, he proceeded to make methodical arrangements for the open air-rest treatment, to which also the more vigorous patients would now be subjected. The wooden porch was torn down and renovated in iron and glass. Soon a second one of similar construction was erected. He also built several large garden pavilions which were protected from the wind. These were all near the house at the entrance to the park.

As regards the winter treatment at Görbersdorf, and in the first years at Falkenstein, both Brehmer and Dettweiler were satisfied with improvement in the medium grades of the disease in the majority of patients of the more robust class who bore the walking and mountain climbing exercises and the inclemency of the weather favorably. With many of the distinctly advanced cases they were satisfied if these passed the winter tolerably well and without particular damage. Later on at Falkenstein, by further perfection of the method, through constant supervision and instruction even to the most minute detail and by the extraordinary results of the prolonged open air-rest treatment, Dettweiler's views completely changed with regard to winter treatment.

The claims of success by Dettweiler and his associates, and by patients as well, increased, and they all became more and more convinced that the winter treatment was just as effective as that of the summer.

A thing which was particularly significant to Dettweiler was the education and better supervision of the patient by the physician, which were first made possible and easy by his treatment. He constantly criticized Brehmer for the latter's laxness in the supervision of patients. Brehmer's patients visited him professionally when they wished, and not at stated times, and it was not until the last years of his life that he remedied this. In the limited time of a visit to a sick room, Dettweiler found it very difficult to give the necessary instructions. These were best and most easily given during the daily visits of the physicians in the rest pavilions. This was a long open gallery protected against rain and inclement weather. He believed that by the general employment of his methods the existing climatic and geographical limitations which had existed until then must pass away; in other words, that the successful treatment of the disease could be carried out anywhere, and that it was not restricted to mountain regions. In this he was entirely opposed to Brehmer and the Davos physicians, who insisted that pulmonary tuberculosis could be successfully treated only in high mountain regions.

Dettweiler's view was completelyc onfirmed by the surprising results of the sanatoria in the mountains with only a moderate elevation, and of those at low levels, and later by the proof at Falkenstein that changes in weather had no observable influence on the course of the disease. His assertion made very early in his career, that the consumptive could be treated with great benefit in his own home climate under suitable open air treatment, has since been completely confirmed.

It may be of value to describe Dettweiler's treatment with some detail. He considered the most extensive sojourn in the fresh air, prolonged fresh air baths, as the most powerful remedy which we possess. A sick man can be hardened by fresh air if subjected to it for a sufficient length of time (*Behandlung der Lungenschwindsucht, P. Dettweiler, Verlag von Georg Reimer, Berlin, 1884, p. 43*). In Falkenstein the treatment was called the "permanent or continuous fresh air treatment." In order to carry it out, special arrangements were necessary. There was constant friendly intercourse between the physician and patient. There was hardly any change of weather which could not be rendered profitable to the patient. On a sheltered terrace, between two wings of the main building, airy glass pavilions and rotation pavilions were built. In these there were about ninety lightly upholstered, bamboo lounging chairs, on which patients with suitable covering passed the entire day except when at meals and walking. All patients lived in the open air in all changes of weather, even in heavy fog, snowstorms and cold at 10° and 12° below zero. Only those confined to bed and to the house by intercurrent accidents or by severe illnesses were excepted. As a consequence of this prolonged winter air therapy, results were astonishing.

During the winter months particularly zealous patients passed from ten to eleven hours of a so called medical day in the open air. Of these there were only a few, probably about six per cent. Eight per cent passed over nine hours daily outside, eight per cent over eight hours, eighteen per cent over seven hours, eighteen per cent over six hours, twelve per cent over five hours, etc. Only a very few were entirely confined to the house on account of advanced disease. There were also only a very few who did not ask for the treatment; these were the highly anemic patients and those with certain forms of continued fever, who were susceptible to chills and high temperatures from even the slightest influence of cold.

Five to six hours in winter was the average for the majority of the weaker patients and those with fever. On account of chills the latter were only able to begin their open air treatment in the afternoon. As a result their treatment ended late in the evening. Behind the beds, arranged in long rows along the walls of the pavilions, gas jets and lamps with reflectors were put up, so that the patients were able to read and write, or play light games. The winter day was often ended at about ten o'clock in the evening and the patient then returned to a cool, thoroughly aired, sleeping room. Dettweiler particularly emphasized the surprising tolerance of the patients against inclement weather and the remarkable diminution in cough and increase in metabolism and also what seemed to be a favorable influence on the fever. When delicate patients began to exercise they were allowed to walk not longer than fifteen to twenty minutes without stopping.

Since Dettweiler was the first to emphasize the fact that phthisis can be successfully treated anywhere, I will go a little more fully into his views. He did not say that every climate, or every change of weather at every location, could be utilized equally well to treat phthisis. Places vary so far as opportunities for catching cold, the possibility of the daily use of fresh air, and the greater or less stimulation of metabolism are concerned. Up to a certain point one can create a local climate, by proper clothing and by building suitable structures; and one can cure the disease in every pure, fresh air, best of all in mountain and forest air. The most diverse forms of phthisis occur in every season of the year. The traditional law of the special usefulness of particular climates was opposed to Dettweiler's experience, and he became convinced that the treatment of phthisis depended fundamentally upon something else than climate, namely upon the individuals and the manner in which they make use of conditions around them.

Dettweiler's views with regard to breathing and mountain climbing exercises are very important. He said that in ordering deep breathing and mountain climbing, one frequently proceeds in a general way and allows patients of all stages of the disease to choose their amount themselves. The lungs are apt to be exclusively considered. We must not forget, however, the very close relation between the organs of respiration and those of the circulation. The dependence of one upon the other is so great that functionally they must be considered together. Every change in the condition of one is reflected immediately in the behavior of the other. Purposeless mountain climbing, which is too frequently ordered in an indefinite way, not sufficiently individualized, and still more frequently carried out in a senseless manner, may have very harmful results on the heart and diseased lung and the entire organism. In hill and mountain climbing we do not have increased work on the part of the lung, which is really only a gas filter. It does not work of itself: it also does not tire, and its relative lack of nerves points to its passive condition. Its function results from the work of other organs, and we are dealing with the work of the entire muscular system, above all that of the heart and thoracic muscles, fatigue of which is immediately manifested by local and general disturbances, particularly of the central nervous system. Every year he had to deplore well marked cases of overexertion of the heart as a result of misused athletic feats, which to the healthy person might seem inconceivably small, and this in spite of the most firmly enforced orders.

During the first periods of treatment he allowed his patients rather too much than too little rest. If there was heart weakness and high grade anemia, every exercise was limited to what was most necessary, intensive rational nourishment was given to the patient, and the entire day was passed on a comfortable bed in the open air, in the shade, and sheltered from the wind, or else in the winter garden. Mild fatigue of the heart muscle often first showed itself after the first smaller climbing exercises had made the patients bolder.

Exertion should be followed only by pleasant after-effects, and a gradual increase in exercise should only be allowed in such cases, and according to the principles *rather more often and shorter than less often and too long*. If after a walk there should occur pallor with slight cyanosis, tendency to dizziness and to yawning, mild tightness of breathing, feelings of discomfort and a more or less troublesome sensation in the region of the heart which will be described differently by every patient, with frequent loss of power of the heart action, absolute rest should be immediately ordered. All further attempts at walking must be forbidden if even a single one of these symptoms be distinctly marked, or are present even by way of suggestion. A single severe fatiguing walk into the mountain which a patient may take too soon, in the glad feeling of returning strength, often throws him back completely. Sometimes the injury is adjusted by some days of greater rest. The ill result occurs more frequently with women than with men, since with the former the condition of anemia and heart weakness occur more frequently.

Deep breathing should always be employed in great moderation and should depend upon the condition of the heart and disease of the lung. At very frequent intervals during the day, the patient should take single deep breaths with closed mouth. While walking and going uphill patients were instructed to take from six to eight deep respirations, at intervals of one to two hundred paces, in such a way that two to three steps be taken for inspiration and the same for expiration, according to the capacity of the lungs. This must be discontinued for a day if there be chest pains which are of muscular origin, or from the tearing of adhesions. If there be a feeling of dizziness and tightness in the breast, one can also conclude that the patient has done too much. The power to breathe deeply gradually increases and the patient observes that he can do his exercises without palpitation and more frequent breathing. The value of deep breathing lies not only in the ventilation of the lung, in the acceleration of gaseous changes, and in improvement of the circulation, but in many in strengthening the thorax muscles, particularly those of the upper aperture.

Dettweiler's bed rest treatment of fever was very thorough (*Die Therapie der Phthisis, P. Dettweiler, Verlag von J. F. Bergmann, Wiesbaden, 1887, p. 27*). He used continuous rest treatment in the open air together with superalimentation. The mouth was used to measure the temperature. He found that the other methods of measuring temperature, for instance the rectal method, caused great inconvenience and interrupted the cure. For all practical purposes mouth measurement was sufficient. Upon the first outbreak of fever, especially if it was of an inflammatory character, he employed absolute bed rest, usually preceded by the administration of a diaphoretic.

While Brehmer is the great outstanding figure in the modern treatment of pulmonary tuberculosis, we would be reluctant to place Dettweiler second in importance to him. In my judgment, Dettweiler had a far greater grasp of the treatment than had Brehmer. The latter, however, was the pioneer and gave the first impetus to treatment. At present, I think our technique in carrying out rest and exercise treatment has improved on Dettweiler's, yet very, very little has been added to fundamental principles as laid down by him.

TERMINAL OR CACHECTIC EDEMA IN THE COURSE OF PULMONARY TUBERCULOSIS

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Observing pulmonary tuberculosis in its terminal aspects, one cannot help but be impressed by the frequency of an edema which cannot be pigeon-holed in the orthodox classification. Presumably the edema of advanced cancer, of Hodgkin's disease, of the primary blood dyscrasias, or of prolonged cachexias from any cause, is of this same, puzzling type. Our personal experience has been solely with the terminal dropsy of advanced phthisis. We realize that in the course of pulmonary tuberculosis the classic edemas may appear, disappear and reappear as a result of well-defined nephritides or cardiac decompensation. With these more or less well understood types we are not, however, concerned. We are interested in a phenomenon so often associated with approaching dissolution, that experienced consumptives who have lived a protracted sanatorium existence have themselves learned to recognize and dread it.

As a result of close clinical observation, we have divided our terminal edemas into three groups: (1) cardiac, (2) nephritic and (3) agonal.

(1) The Cardiac Group: Our experience with this group has been limited. Its members have formed a small minority of our cases. The patients have usually been suffering from tuberculosis for a long time. There has been considerable pulmonary retraction, more extensive on one side. Pleuropericardial adhesions have caused displacement to the more affected side. Definite evidence of cardiac failure manifests itself with cyanosis, dyspnea, orthopnea, and edema. The swelling may begin in the legs or it may be generalized from the onset. The characteristic symptoms are cyanosis and dyspnea. Cyanosis in uncomplicated pulmonary tuberculosis is uncommon. The dyspnea of cardiac failure is characteristic. The patient is obviously, actively panting for breath: his breathing is *labored.* Dyspnea in pulmonary tuberculosis is a relatively mild affair. It may scarcely be apparent that the respira-

tions are accelerated, and the patient may be disturbed only on exertion or when the atmosphere is cold. Arhythmia is, of course, strongly suggestive of a myocarditis, but in our experience arhythmia is rare. As for cardiac hypertrophy, we have never seen a frank instance in our tuberculosis patients, in spite of the frequency of pericardial adhesions and cardiac displacements.

(2) *The Nephritic Group:* Because the edema in this group of cases means the beginning of the end, no matter how long drawn out, it must be included with the terminal edemas. The patient has been sick for a long time; for years perhaps. His illness has pursued a sluggish, chronic course, with pulmonary lesion of the fibroid type. The urine has repeatedly shown the presence of albumin in goodly quantities, with perhaps a moderate number of hyaline and granular casts. It then becomes obvious that the patient's legs are swelling. They are swelling slowly. He feels well, perhaps, and is ambulant. So slowly does the edema develop that it soon ceases to pit on pressure and assumes rather the character of a brawny induration. These patients last many, many months; but eventually they become bedridden, develop anasarca and finally die of asthenia. We can recall no case that exhibited uremia.

This group differs from the ordinary picture of chronic parenchymatous nephritis in several respects: (1) it is not associated with clinically profound cardiovascular changes; (2) the edema is a gravity edema such as is commonly linked with cardiac decompensation, and (3) uremia is rare if it occurs at all. These differences are sufficient to take this peculiar group out of the classical category.

What is the pathology of the kidney in pulmonary tuberculosis? In this connection we can do no better than repeat the frequently cited observations made by Walsh (1) in a careful study of the kidneys at autopsies on 196 tuberculous patients:

> Actual renal tubercles were found in 57 cases (53.8 per cent). Amyloid kidneys were found only 7 times (6.6 per cent) and always associated with amyloid changes in other organs. Of the nephritides, the following were found: acute nephritis, shading from cloudy swelling to marked acute diffuse nephritis, 56 cases; chronic parenchymatous nephritis, 36 cases; chronic general interstitial nephritis, 12 cases; and chronic focal interstitial nephritis 79 cases.

It is noteworthy that Walsh found no instance of chronic general interstitial nephritis due to chronic passive congestion (cyanotic niduration). He emphasized the tendency of phthisical patients to exhibit local scleroses of the kidney rather than widespread interstitial change.

If we return to a consideration of the edema in these cases, we find that the swelling begins in the legs and extends up the body, thus simulating the edema seen in heart failure. How can this be explained? It is apparent that disturbed kidney function depends upon the site, extent and rapidity of development of the lesion. Rapid, widespread kidney lesion results in more or less sudden and complete shutting off of water elimination. Slow damage to kidney function causes gradual accumulation of fluid in the tissues—a sort of very mild anasarca which is not apparent because it is slight. The influence of gravity can then come into play and the fluid seeps through the tissues to the ankles where swelling first becomes manifest. In chronic interstitial nephritis terminating in the cardionephritic complex, any purely gravitational edema of renal origin is overshadowed by that resulting from cardiac failure Moreover, in this type of nephritis, the parenchymal changes are so slight that full function may persist for a long time.

Patients with terminal edemas due to nephritis live a surprisingly long time in spite of the low renal function; for eleven months, in one of our cases.

(3) *The Agonal Group:* This is the most common, most complex and most interesting of the terminal edemas. The clinical picture is sharply defined. A phthisical patient has been gradually, though obviously, succumbing to his illness. For weeks or months he has been bedridden, or partially bedridden, with irregular, intermittent or continuous fever and the supervention of a profound cachexia. There have been no definite cardiac or renal symptoms. Suddenly the patient announces that his legs are swelling. It is usually the patient who makes the discovery. A routine urinary examination at this time may or may not show the presence of albumin and casts. The edema commences most commonly in the loose tissues below the malleoli and over the dorsum of the foot. Less commonly it commences in a puffiness of the face. It may be present one day and gone the next. Soon, however, it persists. It involves one or both ankles, usually both. The swelling can be made to diminish or disappear entirely by elevating the extremities. If the patient lives long enough the edema may extend up the legs, thighs, abdominal wall and back. Edema of the abdominal wall may become so

extensive that it suggests an ascites. But ascites is uncommon. When it does occur, the effusion may be opalescent or chyloid in appearance. In advanced anasarcas, the effects of gravity may be plainly manifest, dependent parts being swollen out of all proportion to the rest of the body. These patients, as a rule, die long before developing general anasarca. In most cases, the swelling is limited to the ankles and perhaps over the sacrum.

Urinalysis may or may not show albumin and casts. In 115 cases of edema, in the course of pulmonary tuberculosis, collected by Montgomery (2), only 36.5 per cent showed albumin. Must we therefore conclude with that author that the explanation of the edema must rest on grounds other than renal?

The absence of albumin and casts does not necessarily exonerate the kidney. Thanks to the excellent researches of Hedinger and Schlayer (3) on kidney function and Mosenthal's simplification of the technique (4), making it available clinically, we have been able to study our edema cases from a new angle. Definite evidence of changes in renal function can often be obtained when anatomic lesions are not demonstrable in the form of albuminuria or the shedding of casts. Our edema cases, whether they were associated with an obvious nephritis or not, showed definite functional changes, notably in a loss of specific gravity flexibility and a deficient elimination of chlorides. Our results with the renal functional test in terminal edema confirm the findings in two cases investigated by Mills and Henderson (5). While these findings were constant in all of our agonal edemas, we must not overrate them and hastily condemn the kidney on the basis of renal functional tests. In some respects "renal function" is a misnomer as applied to the two-hour test. Even with characteristic findings the fault may not be in the kidneys primarily. Mosenthal has shown that the same picture of fixation of specific gravity and diminished excretion of fluid and salts occurs in cardiac decompensation and other extrarenal conditions. Under these circumstances, the fluid and salts never reach the kidneys; hence these substances cannot be eliminated.

We have noted that in the agonal group the edema apparently begins in the ankles and extends up the body. To what extent is the picture cardiac? Doubtless the heart shares in the damage caused by the toxemia of progressive phthisis. Undoubtedly, recognizable anatomic changes are present in the myocardium. But we must not hide behind the convenient but often meaningless diagnosis of myocarditis. To paraphrase Krause, myocarditis may "really explain a lot if you have outlived your youthful insistence for sharpness, clarity and definiteness." In our agonal group of terminal edema the picture is not cardiac by any stretch of the imagination. Edema of cardiac origin can only result from failure of the circulation. Where are the concomitant symptoms: labored breathing, orthopnea, cyanosis and chronic passive congestion of liver and spleen? If there is a clinically worth while myocarditis, how can we account for the singular absence of arhythmia? It would therefore seem that we can definitely rule out the heart as an important causative factor in agonal edema.

Aside from the heart, other extrarenal influences, which might be responsible for a failure to eliminate fluids, are the lymphatic circulation and changes in the body tissues. Given an adequate circulation of the blood and there will be little reason to suspect failure of the lymphatic circulation unless there is definite obstruction. If the lymphatics were primarily at fault we might reasonably expect the more frequent appearance of ascites. The chyloid ascites sometimes noted resembles chylous ascites only physically. The effusion is characteristically free from fat, the peculiar opalescence being probably due to lecithin bodies. Subcutaneous injections of phenolsulphonethalein were rapidly absorbed, carried into the circulation and often rapidly eliminated by the kidneys in some of our agonal edema cases, thus exonerating the lymphatics, the heart and the kidneys in so far as the absorption, transportation and excretion of dye are concerned. It is possible that waterlogging of long standing may interfere with the lymphatic circulation secondarily. On the whole, we feel that the lymphatics play a minor rôle, if any, in the production of terminal edema.

Apparent renal failure may be secondary to changes in the tissues themselves. In the past few years, biochemical studies, notably those of Fisher (6), have demonstrated that colloidal substances under certain circumstances possess the property of imbibing water. If gelatin be placed in water it will absorb a certain quantity and swell: if this water is slightly acidulated, the swelling is markedly increased. If the eyeball of an ox be placed in water moderate swelling occurs: if the water be acidulated the eye soon becomes tense to the bursting point. If the leg of a frog be ligated tightly above the knee and placed in water, marked swelling of the ligated limb occurs after from twelve to twenty-four hours: a similar experiment with a dead frog results in the swelling of both limbs, in fact, of the entire body. The human body, left in water after death, becomes markedly edematous.

A relationship between these experiments and clinical edema is suggested by the fact that edema fluids have been found acid even to such a coarse indicator as phenolphthalein; by the presence of an increase in the carbon dioxide of the blood and the appearance of abnormal acids, in the urine lactic acid, for example.

In our agonal group of cases we can apparently rule out the heart, kidneys and lymphatics. These patients are usually profoundly toxic, while aeration is defective as a result of lung destruction and perhaps also because of a sluggish, low-tension circulation. Whether a state of acidosis exists remains to be determined and results will be reported in a subsequent paper. At any rate, we would appear justified in suspecting predissolution disturbances in the tissue metabolism, resulting in the production of acid or other bodies favoring the conversion of hydrophobic colloids into hydrophilic colloids. The end result is an edema varying in intensity with the degree of tissue injury. The edema may be so slight that it may not be obvious except in dependent areas. As a matter of fact, there probably exists a state of anasarca from the very start, but not obvious until there is sufficient accumulation. Even in marked cases one can get parts of the body free from edema by elevating them. It is a common experience to see one limb markedly puffy while the other shows not a trace of edema. And this phenomenon is reversible by a change in position of the patient.

We have shown that there is a constancy of renal function in the agonal edemas,—fixation of specific gravity, chloride and water retention and usually a nocturnal polyuria. But this may be secondary to generalized tissue change—and may also explain the absence of any pathological changes in the kidney on postmortem examination.

STATISTICAL AND FUNCTIONAL RENAL STUDY OF THE TERMINAL EDEMAS

In consulting the histories of 181 patients who died in the Sanatorium from the beginning of 1916 to October, 1919, we find that 17 developed an edema shortly before death. But we must include in this record 2 cases which became edematous while at the Sanatorium and are known to have died shortly after leaving the institution. Roughly, then, about 10 per cent of all our deaths are associated with a terminal edema. In addition we have studied 6 cases, still in the institution, but which, for prognostic reasons, may be considered as terminal edemas, thus bringing our total to 25.

Of the total number, 4 may be classed as cardiacs and 9 as nephritics, while the remaining 12 belong distinctly to the agonal group. The most long-lived were the nephritics averaging six months (lowest, six weeks; highest, 11 months). The cardiacs averaged three and one-half months, while those of the agonal group averaged two and one-half months. Of the 19 cases that died, 9 had general anasarca (3 with ascites), while in 10 the swelling was below the knees. Of the 6 cases in the house, 1 has a large ascites and a general anasarca, 1 has puffy face and ankles, while 4 are edematous only below the knees. In the total of 4 ascitic cases, 3 were of the chyloid variety.

It is interesting that in 2 of the cardiac cases there was a rapid, general anasarca resembling that of acute nephritis.

Amyloid liver was diagnosed in 4 out of the total of 25 cases. In 3 the liver was moderately enlarged and hard, with surface smooth and edge regular, thin and not lower than the umbilicus. In 1 case the liver was enormous, reaching from the fourth interspace to the right iliac region, with marked bulging of the lower ribs and epigastrium. Unfortunately, we were unable to secure permission for autopsies on any of these cases. The spleen was probably enlarged in 2 cases although palpation was confusing because of the enlarged left lobe of the liver.

Functional renal tests were done on 11 terminal edema cases and on 10 controls. The patients were put on a regular house diet, with the addition of a glass of water every two hours and the administration of two 10 grain capsules of sodium chloride after every meal, beginning with the evening meal of the day previous to the test. A specimen voided at 8 A.M. was discarded. Two-hour specimens were then collected up to and including 8 P.M., and a night specimen was obtained from 8 P.M. up to and including 8 A.M. Each specimen was measured, the specific gravity taken and an estimate made of the chloride excretion in the total day and total night urines, using the Volhardt method. In all but 6 a phenolsulphonephthalein renal function test was done.

In all but 1 of our terminal edema cases there was more or less fixation of the specific gravity from two to five points, the nephritic cases running on a somewhat lower specific gravity level than the agonal group (1015 as compared to 1020). In one definitely nephritic case there was a specific gravity variation of nine points. All showed a drop in the specific gravity of the nocturnal specimen as compared to the day specimen, and a relative nocutrnal polyuria. The total fluid output was moderately diminished, averaging 1200 cc. in twenty-four hours, the fluid intake being 1700 cc. In one case a polyuria resulted (2100 cc.) which was chiefly nocturnal (1500 cc). The phenolsulphonephthalein excretion was diminished in all but 2 of the edema cases, both exceptions being in nephritic types.

Functional renal tests were not done on the 4 obviously cardiac cases. In the agonal and nephritic groups, change in the renal function was constant.

We have seen that renal failure may develop insidiously in old fibroid patients running a sluggish, often apparently inactive, course. In the presence of this continuous, low grade toxemia, can such supposedly quiescent cases really be considered quiescent, and would not periodic functional renal tests cast some light upon the prognosis?

SUMMARY

The terminal edemas of phthisis present themselves in three clinical groups: (1) cardiac, (2) nephritic, and (3) agonal. The cardiac group is a small group in which the edema may simulate the rapid anasarca of acute nephritis, or appear slowly with an accumulation in the ankles, gradually extending up the body. In this group we should insist on definite evidence of cardiac failure. The nephritic group occurs most commonly in chronic fibroid cases of long standing with apparently latent pulmonary lesions. The characteristic renal change is focal sclerosis. The gradual failure of the kidney to eliminate is the probable explanation of an edema simulating the cardiac type. The agonal group of edemas is probably caused by predissolution metabolic changes in the tissues themselves, resulting in the conversion of hydrophobic into hydrophilic colloids. The kidneys show secondary changes in function.

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SOME CONSIDERATIONS REGARDING THE DIAGNOSIS OF PULMONARY TUBERCULOSIS[1]

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The great clinical teacher, Gee, had a saying that the first part of medicine was Diagnosis, the second, *Diagnosis*, and the third, DIAGNOSIS. This saying is perhaps less applicable to pulmonary tuberculosis than to most other parts of medicine, for here treatment seems a matter of greater importance than diagnosis, and, perhaps, of greater difficulty. If one were to attempt the ungracious task of judging where and how his medical brethren come short, it would, I think, be found that more mistakes are made in the treatment of pulmonary tuberculosis than in diagnosis, and more in prognosis than in both together. However, whether in first or second place, any discussion of diagnosis, if well informed, must always be fruitful.

The means and instruments at our disposal are constantly changing and our modes of thought as well. Many of us who have been thinking tuberculosis for ten or fifteen years, that is, a medical generation, have considerably changed our working ideas. It is not so much that we have discarded facts and opinions of ten years ago as that we have rearranged them and place the emphasis differently. We look at the old and new facts from a new direction.

Ten years ago the burden of all papers on diagnosis was that it should be made early and ever earlier: now the burden is that the diagnosis should be made accurately and ever more accurately. Heavy at that earlier time was the judgment upon him who failed to make the diagnosis when it should be made, but much lighter, fortunately for many of us, upon him who made the diagnosis when it should not have been made at all. Tuberculous infection, considered to be almost universal, was not always clearly distinguished from tuberculous disease, fortunately by no means so universal. With a background of almost universal infection we were inclined to fill in gaps in the outlines of disease in the foreground. Tuberculous was easily presumed, and the onus was on him who would *un*-make, not on him who would make, the diagnosis. If we missed the bull's-eye, or even the actual target, we had some satisfaction in having at least hit the barn door upon which it hung.

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[1] Read before the Medical Society of Winnipeg, Manitoba.

The pendulum has swung far, possibly too far, in the other direction. Perhaps we have become too critical of proofs of diagnosis in a disease so insidious in its onset as tuberculosis. There is some sign of a return swing, of a fuller appreciation of the almost imperceptible gradations by which latent and potential disease may become actual and active disease. But, however our views may change, the extra emphasis placed during the past few years on accuracy in diagnosis has meant great and permanent gain.

Three causes or three teachers have had chiefly to do with helping or driving us toward closer diagnosis: first, the war; second, the pestilence—the influenza epidemic; and third, the fuller application of the X-ray to chest work. In the period of enlistment the closest possible diagnosis was necessary, that the unfit should not be driven into service and that the fit should not be allowed to shirk. And soldiers came back from the war with so many kinds and combinations of pulmonary disabilities, that, after a period of bewilderment, we grew, perforce, to differentiate better. We were taught in spite of ourselves. And when we began to see our way a little through the pseudotuberculous conditions following war service, to these were added the various dregs of influenza, even more bewildering. Fortunately we had, in the improved and more fully appreciated X-ray plate, a new ally, which not only helped in diagnosis and checked our findings through other methods, but also taught us widely and deeply regarding pathology.

It was said by the Greatest of Teachers that "An evil and adulterous generation seeketh after a sign." Physicians, though not an evil generation, do certainly seek after signs, clear marks of disease, means of automatic diagnosis, easy shortcuts. History taking is laborious, physical examination time-consuming, and judgment difficult. The hope we have of each new measure is that it will make the diagnosis more easily and directly, announce a result like handwriting upon the wall, or bring a sure decision from the laboratory worker by return mail. But to this wise generation of ours, as to the simpler one of older days, signs that are easy, clear-cut, automatic and fool-proof have been vouchsafed very rarely. The best a new procedure can do is to enable us to make our diagnosis surer and earlier, even if not easier. The easier the diagnosis the less usually is its value and the worse the prognosis. When the neighbors can make a diagnosis from across the street its value is about nil and prospect of recovery about the same. The diagnosis in pulmonary tuberculosis is not made more easily than it was ten years ago, but it is made more accurately and is of greater value when made.

HISTORY

If a choice had to be made of one element only in the diagnosis, the choice would be not physical examination, nor X-ray plates, nor laboratory tests, but history. Perhaps the pen is mightier even than the stethoscope.

The history must be a full one. If a man suffers from a broken leg or a child from scarlet fever the significant history elements are few and easy to get, but the beginnings of tuberculosis are involved in all a man has ever been and done; in his parentage, associates, housing, work, play, habits, wages, temperament, nationality, social conditions and travels to and fro. It is a part of all that he has met.

Twenty years ago family history was considered important because hereditary transmission was believed in. It is important now, though hereditary transmission is not believed in, because of family contact which is the earliest and most constant, and also, perhaps, because of inherited predisposition.

There is no more important element in the history than the record of previous illnesses. Acute respiratory diseases of all sorts; "colds," grippe, "flu," which are easily confused with tuberculosis, or may very definitely open the door for tuberculosis; typhoid fever which gives something like a double chance of tuberculosis breakdown in the five years following attack, and for which acute tuberculosis has often been mistaken; digestive disturbances and nervous conditions which may be confused with, or be symptoms of, or may definitely lead to, tuberculosis breakdown; pulmonary diseases of all sorts—pneumonias, pleurisies, asthmas, spells of hoarseness, all must be canvassed and recorded.

While in most diseases the time of infection and the time of onset of symptoms are separated by a brief and fairly constant interval, in tuberculosis the interval may be a few days or two score years. This interval must be reconstructed, filled in, charted, the events pieced together by careful enquiry, and the course of the disease thus outlined. The date of earliest manifestation is most important. It is remarkable, once the diagnosis is made, how many old slight illnesses can be strung on the tuberculosis string.

General conditions, social, industrial, community and personal, have already been mentioned. A most important enquiry, even with diagnosis in view, is that with regard to work, amusement, recreation, rest, income and output of energy, and conservation or dissipation of strength. A chief cause of health breakdown is the overspending of energy, more usual in so called play than in work, more usual in unnecessary than in necessary effort, more usual after six o'clock than before it. Many so called recreations do not re-create, do not restore the balance after labor, but rather dissipate energy until natural fatigue after labor becomes unnatural exhaustion after play. The social pace a woman sets herself, the amount of her nonessential activities, forms a much more important element in her history than the amount of her proper housework or the diseases her grandparents died of. A carefully taken, searching, complete history gives an understanding of the general outlines of the case and means both diagnosis and prognosis half made.

SYMPTOMS

In the days of not so long ago we spoke of pathognomonic signs and symptoms, but he would indeed be bold who would now say of any sign or symptom that it belonged definitely to tuberculosis. As Thomas McCrae pointed out, and as all agree, soldiers in the trenches had cough, expectoration, weakness, loss of weight, elevation of temperature, blood in sputum, night sweats, dulness on percussion and râles and pains in the chest, and yet were not definitely tuberculous. When all the classical symptoms of a disease taken together cannot definitely make a diagnosis, and yet each one is important, the difficulty of interpreting symptoms can be realized.

Cough is such a classical symptom. It is not a big cough. The man who is "coughing his head off," is likely nontuberculous or has a nontuberculous complication. The man who clears his throat habitually, but denies that he has cough, or whose friends have noticed a slight hack becoming more frequent, is much more likely to be tuberculous. His cough will be more marked on rising in the morning, after meals, and on retiring, but this is characteristic of most coughs, and so scarcely diagnostic. And definite tuberculosis of the lungs *can* be present without a noticeable cough.

Expectoration (that is, of course, *ex-pectoration*, something out of the chest, and not postnasal or antrum discharge) in early stages is usually scanty, with a little yellow in it. Mucoid or tenacious expectoration, profuse expectoration when there is no cavity, or in the absence of marked symptoms, profuse expectoration as the outstanding feature of the case, or bad smelling expectoration, are not typical of tuberculosis.

Dyspnoea, usually slight, will likely be found in early tuberculosis in proportion to impaired strength, lassitude and toxemia, rather than in proportion to destruction of tissue. It may be more noticed at an early acute stage than at a moderately advanced, more chronic stage. Marked dyspnoea, when the general condition is good, and dyspnoea as the prominent symptom, point rather to nontuberculous than to tuberculous disease. The man who tells you he finds his breath short when running to catch a car may be tuberculous, but the man who is short of breath on an ordinary walk, with other signs or symptoms not marked, likely is not.

Freer perspiration than usual—often associated with overclothing—is of some diagnostic value. Such will often be wrongly described as a night sweat. The real night sweat, toxic in origin, cold, clammy, drenching and bad smelling, is a text book symptom, is rare in even advanced cases on a proper routine of rest and in the open air, and is of no use in diagnosis.

A characteristic *rise of temperature* is most useful in diagnosis of early tuberculosis. To go through the form of taking the temperature is easy; to make the necessary allowances and draw the right conclusions, to estimate correctly the body heat of the patient, is by no means so easy.

There is no normal temperature, but varying normal temperatures for different individuals, ages, temperaments, sexes and races, times of the day, occupations. There are differences before and after meals, before and after sleep and in women at different phases of the menstrual cycle. There are added difficulties in that we are trying to measure on the *outside* of the body the temperature of the blood stream *within*, with thermometers of which few are instruments of precision. The only temperature-taking of real value in early tuberculosis is not at the clinic or the doctor's office, but in a hospital ward or in the patient's own home, with a good thermometer, held in the closed mouth twenty minutes, at a considerable interval after meals, and after at least a short period of rest; taken at regular hours in the day for at least a week and the results recorded. As frequently taken, hurriedly, under excitement, and without appreciation of conditions or allowances, in a doctor's office, a temperature record cannot be much depended on, may be most misleading, and gives only approximation rather than exact mensuration.

Even after a slight, persistent elevation of temperature has been established, other pathological conditions in bad teeth, tonsils, gall bladder or intestine, in thyroid hyperactivity or even simple constipation must be ruled out.

In early tuberculosis the *pulse rate* becomes usually more rapid and excitable. *Blood pressure* is inclined to be low. Usually there is *pallor* and a flush, with a slight fever. An unusual *sensitiveness* to low temperatures is often noted, even if the body temperature is normal, the patient saying that he "feels the cold much more than usual." Temperature variations about the menstrual time are more exaggerated in tuberculous than in healthy women. *Irritability* and nervous instability are not infrequently elements in the picture. *Digestive disturbances* are often early and confusing symptoms. *Lack of appetite* is often a lack of morning appetite, a disinclination for breakfast. Patients with early tuberculosis are often ten pounds below their normal *weight*, and their normal about ten pounds below the normal for their sex, height and age. *Weakness* is better described as "becoming tired or playing out more easily than usual." *Tiredness* is frequently morning tiredness, disappearing in midday and felt again in the evening. The night has not been long enough to clear up the work toxins of the day plus the disease toxins. While lassitude is characteristic, it may alternate with unusual excitability and even exhilaration. The toxins can stimulate cerebral activity.

COMPLICATIONS

Apart from symptoms proper, some conditions which might be classed rather as complications have a definite diagnostic value. In this class is the *ischiorectal abscess* which in from fifteen to thirty per cent of its occurrence is tuberculous or associated with tuberculosis.

Haemorrhage from the lungs occurs in nearly fifty per cent of cases of pulmonary tuberculosis and sometimes is the first noticeable symptom. As has been said, a haemorrhage may be the end of the beginning or the beginning of the end; that is, some early and some late, some diagnostic and some prognostic. There are other causes of haemorrhage, such as spongy gums, bad teeth, cardiac conditions, lues, vicarious menstruation, carcinoma, sarcoma, bronchiectasis, abscess, etc., but the outstanding cause of a frank haemorrhage of a drachm or more of blood, especially in a fairly young person, apart from gastric ulcer, is tuberculosis. Shreds and streaks and clots of blood, which strike terror to the hearts of neurasthenics, are usually to be disregarded.

Ten years ago *pleurisy*, especially with effusion, was as clearly diagnostic of pulmonary tuberculosis, almost, as hemoptysis. Ninety per cent or more of pleurisies with effusion were considered definitely tuberculous, and the others most suspicious. Pleurisy ten years ago was tuberculosis. Pleurisy to-day is—pleurisy. After all has been said, however, pleurisy, especially with effusion, and especially if recurrent, though not absolutely conclusive, is one of the most convincing elements in the diagnosis of tuberculosis. It should indeed make the diagnosis and determine the prognosis—unless an alibi can be proved.

Disease in the larynx is secondary to disease in the lungs, but a husky voice is often the earliest danger signal of lung disease observed by the patient. Early laryngeal tuberculosis is better detected *from below upward* than *from above downward*, that is, the diagnosis should be made on very slight throat signs if the lungs are diseased. To wait for an unmistakable throat lesion is to wait much too long.

Skin manifestations of tuberculosis, not lupus, but the various tuberculides, are rare and not well known. While the papulonecrotic type is pretty definitely a sign of tuberculosis, more usually of a hidden not very active focus, the erythema nodosum or induratum type may be, and likely is, associated with other conditions as well, tuberculosis supplying only one of the toxins by which it is excited.

PHYSICAL EXAMINATION

Physical examination is, always has been, and always will be, important but it is by no means the whole of diagnosis. Ten years ago it was overestimated, and papers on diagnosis were very largely considerations of elaborate methods of physical examination. Many diagnoses of that time, like inverted pyramids, poised unsteadily on their apices, and rested upon only slight variations in chest sounds. Basing an important judgment upon a slight variation from normal presupposes an exact and invariable normal which does not exist in the chest and a niceness in appreciation of physical signs which few attain. As many mistakes may have been made by the overvaluation of chest sounds as by their undervaluation. The best diagnostician is not the man with the keenest ear and the most sensitive touch but the man of the sanest and best informed judgment. Diagnosis is a mental and not a physical process.

Careful and methodical percussion has not been superseded by any of the newer methods, and is still of value. Auenbrugger's chest thumping, to which his patients and friends submitted reluctantly, suffering soreness thereafter for days, has given place to a percussion very much gentler and at the same time more valuable. The finger receives more impressions than the ear. Unfavorable conditions, such as downtown street traffic, affect percussion much more than auscultation.

Abnormal chest sounds are of two kinds, abnormal variations in sounds normally present in the chest and secondly, wholly abnormal sounds. In examination we first listen to sounds as they are on normal breathing, and then take special means of producing sounds. The most important of such measures, without which no examination is complete, is the production of râles in inspiration following cough after expiration. After we have listened to both ordinary and extraordinary sounds, we may enquire, first, if the sounds are sufficiently abnormal to show disease present, and, second, as to *what* disease is so shown. Râles in the chest, even many moist râles, do not necessarily prove tuberculosis. A whole lung full of bubbling râles may indicate septic bronchitis due to diseased sinuses, and needs the care of a nose and throat specialist rather than treatment in a sanatorium. Certain crepitations, especially along bases, need not be pathological. As Lawrason Brown has well said, basal crepitations, even if pathological and fairly extensive, are to be considered nontuberculous until the contrary is proved, while apical crepitations are to be considered tuberculous until the contrary is proved. Musical sounds in the chest are usually nontuberculous. Atypical râles are usually nontuberculous. The importance of any physical sign is increased by its persistence in one area. A onesided condition is more apt to be tuberculous than one which is bilateral. Signs and pains which wander are likely nontuberculous. Muscle sounds, shoulder joint sounds, heart sounds, pericardial sounds, the rub of the stethoscope on the chest skin or, still worse, on the chest hair are common sources of error. No sign is pathognominic. At the same time definite, localized, typical, apical râles are second only to bacilli in the sputum in definiteness.

Auscultation, discovered by Laennec one hundred years ago, remains preëminent among methods of physical examination.

Vocal resonance and fremitus, and the measurement of the chest, give information rather for differential and late diagnosis. Physical signs should not be definitely stated to be absent until after a second examination. One is never entitled, even after a very searching examination, to say "There are no abnormal signs," but only, "I have *found* none." A physical examination in a noisy downtown office with a dozen waiting patients cannot be satisfactory. The patient must be stripped to the waist and the lower costal margins be quite clear of all entanglement. Findings should be recorded, not only in order to make them available for later use and comparison, though that is most important, but to give the findings a clearer definition in the mind of the examiner at the time. "Writing maketh the exact man," in physical examination as in anything else. An examination recorded is worth twice as much at the time, and ten times as much in after-remembrance as one unrecorded. The pen and the stethoscope go well together.

One who has not had opportunity for experience in the niceties of physical diagnosis will make fewer mistakes if he usually, though not always, requires a definite click or râle before making the diagnosis. While the slighter variations that border on the imaginary are discounted much more heavily than they used to be, we should have as wholesome a regard as ever for the localized, persistent click, even slight, especially near the apex.

THE ROENTGEN RAY

When X-ray apparatus reached a perfection that made good stereoscopic plates possible, medical men, still looking for a sign, and weary of the old routine, said "Eureka!" But while this new aid to diagnosis ranks with the stethoscope of Laennec and the Koch bacillus, it is not the automatic fool-proof sign we longed for. It is just one more witness come to court.

The fluoroscope is especially useful in differential diagnosis and in estimating the results of pleurisies, the extent and significance of adhesions, and movements of the diaphragm, and for following the treatment by artificial pneumothorax it is invaluable.

But in the diagnosis, especially of early chest conditions, the plate is the thing. And it must be a good plate, stereoscopic, and taken and developed by perfect and uniform technique.

Given, then, the perfect plate, that is, the dream, what is the interpretation thereof? The plate is silent. It does not tell its own story. It shows shadows mingled and superimposed. It is as confusing as the pathless forest to the lifelong denizen of city streets. It baffles and bewilders him. To the practised woodsman every turn of a leaf and every mark in the snow tells its story; to the man of the streets they tell nothing. Many a day will pass before he knows the voices, the tracks, the haunts, the writing, and the laws of the forest in all their changing phases throughout the seasons. It has been said of a chest plate that it represents "a pitfall for the inexperienced, a problem for the trained observer, and a harvest for the charlatan."

It would carry one into a subject quite large enough for many papers to attempt to discuss details of X-ray diagnosis. One difficulty is that there is no such thing as a normal plate. Again, the plate records not only the pathology of present conditions, but to some extent every cold or grippe or bronchitis or old infection since the beginning of life. The extent and variety of shadows, thickened basal trunks, heavy hila, small opacities and haziness which can be present without proving present tuberculosis, are always a source of wonder to the beginner. What significance to allow to peribronchial thickening is always a vexed question.

The plate does not make the diagnosis. It helps to make it. It is a witness, but not judge and jury. Those who best know chest plates are least dogmatic. The question as to which is supreme, the plate or the stethoscope, is beside the mark. They are complementary means of examination and most efficient when used side by side, so that the story of each may be called for alternately. Ancient history, and, at the other extreme, disease of the most rapid type, are better shown by the plate than by the stethoscope.

BACILLI

Ten years ago we were accustomed to say with much emphasis that a diagnosis made by finding tubercle bacilli in the sputum was made too late. By that time the earliest stages of the disease had been passed and one who had to wait so long was a bankrupt diagnostician. With the increased scepticism of recent years, however, and the greater difficulty in differential diagnosis since the war and since the influenza, the finding of bacilli has become more important than ever before. After all has been done, the diagnosis will in many cases be more or less in doubt until bacilli have been found.

While the finding of bacilli about which there can be no question gives very definite information, it cannot be too often or too strongly stated that a negative finding cannot unmake or interfere with a diagnosis. A sputum examination is not a chemical test; it is an exploration. When there is any reason for a sputum examination, there is reason to examine unto seven times and even unto seventy times seven and by many methods. One fish caught proves fish in the river, but a hundred failures do not prove no fish in the river.

Brown has well said, "Failure to find and to interpret aright physical signs may be excused, but failure to ask for and examine sputum cannot be condoned."

TESTS

Complement fixation, though it is said to give additional information, and to be another witness with circumstantial evidence to offer, does not seem to be as yet, at any rate, the sure sign looked for by this eager generation.

The tuberculin test seemed for a time the certain sign looked for,—as plain as the handwriting on the wall. Then were found its limitations, that it gives much less than a complete automatic diagnosis, that it does not say unequivocally "yes" or "no," and cannot decide between tuberculous infection and tuberculous disease, tuberculosis old and historical, and tuberculosis present and active. It is really a measure of sensitiveness and that is about all.

The uniform rather large dose of tuberculin, frequently given as a test, is a mistake. A reaction to ten milligrams is a very different matter from a reaction to one one-hundredth of that amount to one-tenth of a milligram. If we are measuring our patient's strength it is more useful to know that he can be knocked down by a feather than to know that he can be knocked down by a club. It is the part of wisdom to try the feather first. A mild reaction to ten milligrams does not diagnose present active disease, does not show need of treatment, and is, in an ex-soldier, no basis for pension. A fairly marked reaction to a much smaller dose carries a different implication. Even if tuberculin cannot make out the whole case, when used as a measure of sensitiveness, with care and a full knowledge of its variations and limitations, it is a useful witness and should be called into court more often than it now is.

DIFFERENTIAL DIAGNOSIS

That there may be difficulty in differentiation between early tuberculosis and other conditions such as anaemia, malaria, acute respiratory diseases, goitre, neuroses, postinfluenzal debility, etc., may be easily appreciated, but that the late stages present almost if not quite equal difficulty, or perhaps greater difficulty, may be to some a hard saying. McCrae and Funk in wards for far advanced tuberculosis cases in Philadelphia found something like five or six per cent nontuberculous. It is doubtful whether many wards for far advanced tuberculosis cases would show as *small* a percentage of nontuberculous.

As has already been stated, the war and the influenza epidemic have added to the difficulties of differential diagnosis. Among the confusing conditions are pleural infections of all sorts and degrees, empyemata, large and small in all sorts of pockets, with and without bronchial fistulae, and in all stages of repair, bronchiectases, pulmonary abscesses and other septic conditions, bronchopneumonic and pneumonic processes, bronchial asthmas of many varieties and causes, the after-effects of gas poisoning, and the whole family of bronchial conditions characterized chiefly by dyspnoea, weakness, chest discomfort, emphysema and susceptibility to "colds."

Preëminently, the chest condition of the returned soldier who has seen much service is chronic bronchitis, associated in his mind more with service in England than with service in France. There is a general dulness on percussion, wheezy rhonchi and basal crepitations are heard, and plates show marked peribronchial thickening, especially at the bases.

In making differential diagnoses among conditions characterized by pretty much the same signs and symptoms, the proportion of signs to symptoms or symptoms to signs becomes important. In nontuberculous conditions, usually, signs are more impressive than symptoms, the duration longer, and general health in proportion to signs and symptoms better than in tuberculosis. The ordinary pigments red, yellow, blue, green, purple, in one combination make up a landscape, in another a seascape, in a third a portrait. So, a group of symptoms and signs and elements— cough, expectoration, dyspnoea, pain, wheezes, râles, chronicity—in one arrangement in one set of proportions makes a recognizable picture of bronchiectasis, in another a plain picture of tuberculosis. The differential diagnosis is made by the characteristic grouping of elements of diagnosis rather than by the mere presence or absence of elements.

So far, the physician has been pictured as examining various witnesses, following clues, collecting evidence, investigating, piling up data. The patient had been put into the dock and crossquestioned as to all he ever was or did or suffered; from the physical examination the last fact has been extracted; the X-ray plates have been quizzed over and over; the sputum has been examined and reëxamined; tuberculin, it may be, has been brought in to give its evidence; and all the witnesses, small and great, who have anything to say, have said it. Many cases practically plead guilty, almost without trial, by showing bacilli in the sputum or a definite combination of elements of diagnosis. But in many cases—of which there seems to be an evergrowing number—the decision is in doubt. The physician then must be judge and jury, and the widest experience and the best diagnostic judgment he can bring to bear are by no means out of proportion to the task of reaching a verdict. Even then,—but we trust in an ever-decreasing number of cases as time goes on,—we must be satisfied with a probability diagnosis or the old cautious Scot's verdict of "Not proven."

THE PREVENTION OF TUBERCULOSIS BASED ON THE RELATION OF CHILDHOOD INFECTION TO TUBERCULOSIS IN ADULT LIFE[1]

ALLEN K. KRAUSE

From the Kenneth Dows Tuberculosis Research Fund of the Medical Clinic of the Johns Hopkins Hospital and University

Available data can hardly warrant an extreme position on the dictum that manifest, adult, human tuberculosis, particularly of the lungs, is the fruition of an infection acquired in childhood. Against the familiar facts that most city children become infected, that infection confers an immunity to reinfection, that infection is almost habitually notoriously persistent and that primary outbreaks of clinical tuberculosis can frequently and with unexceptionable proof be shown to have emerged from a background of years-old infection can be opposed the equally well-authenticated circumstances that tuberculo-immunity is never more than relative, that it declines as lesions becomes more sclerotic and, therefore, less susceptible to activation, that tuberculous infection (lesion) is not necessarily permanent, that both experimental and clinical observation prove that lesion may become sterile and thoroughly eradicated, that in this event immunity disappears, that the remarkable divergence of localization of pulmonary infection and disease suggests that the more peripheral lesions of adults represent reinfections from without if we would hold to the inhalation concept of lung infection, and, finally, that all animal experimentation proves, not that infected immunes cannot be reinfected, but that the results of reinfection are a modified tuberculosis, more localized, more chronic, yet on occasion still very protracted, as compared with the course of virulent infection induced in a nonimmune.

Estimates, then, of what proportion of adults fall ill from post-puerile infection and what ratio from childhood exposure are usually founded on bias and imagination. We have no way of accumulating the evidence

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that will give them scientific weight. No one has yet kept careful records from infancy to and through adolescence, of the ups and downs, the appearance, disappearance and reappearance, of the Pirquet reaction, that index of infection, in only ten of the millions of infected children. It may be that for longer or shorter periods we would find that a large proportion would exhibit nonreactivity, and therefore noninfection, where reaction and infection had been shown before; and further that many of these would later again give the test of infection,—in their case, reinfection. What little has been done in the way of prolonged and continued observation of the individual child's response to infection tests—and it is little enough—has been concerned with clinic children, most of whom were under observation for an infection which had become so well established, had developed to such a point, that illness or abnormality was noticeable; and we must admit that the possibilities of the subsequent course of infection in these children would be quite different from those of the very slight and presumably transient infections that might follow the almost negligible exposures which many others experienced.

But all this is speculation, even though it attempts to take into account compelling consequences of scientific observation and social and family relations; and would indicate, also, only one or two of many wide gaps of knowledge which must be filled before we may become too dogmatic about the obligate development of adult tuberculosis from childhood infection.

Yet, that childhood infections are prolific breeders of adult tuberculosis cannot be denied. Anyone who comes in contact with many adult consumptives needs no better evidence of this fact than good and thorough histories, which he has pieced together after adroit cross-examination of his patients. Scores of these will satisfy every requirement laid down by the most uncompromising proponent of the puerile genesis of adult disease, and physical examination as it brings to light anatomic evidences of hidden, always silent and never-suspected residua, will not infrequently clinch past history.

So much seems uncontrovertible. The limitations of time forbid the arrangement of reasons which urge belief in the truth of another proposition which is pertinent to my subject, the proposition that tuberculosis infection, once established, responds to the tissue activities which are set in motion by all events which enter into human experience, or, more concretely expressed, that factors of environment and inheritance through their effects on the tissues of the body and thus on tuberculous lesions which the latter environ, exert a determining influence on the course of infection. Under their interplay, combination and balance, infection advances and retreats, comes to light as clinical disease or is dampened into inactivity or smoulders in obscurity, for longer or shorter periods, indolently or fulminantly, continuously or haltingly. Since the wellsprings of inherited factors are largely beyond our control, these will receive scant attention; their effects are, moreover, modifiable by environmental factors. Therefore, within the short compass of this paper I wish merely to enumerate a very few of many measures which would promise a reduction of that adult tuberculosis morbidity which develops from childhood infection, a few measures which may seem practicable of application.

These measures would take the incident of infection for granted and proceed with the sole purpose of preventing at any time its development, or restricting this to a minimum. It is fair to assume that if all infection were kept thoroughly inactive throughout the years of childhood it would become so sclerotic and well invested that practically no adult disease would develop from it and that, what is more significant, much more of it would completely die out.

It should hardly be necessary to point out that, taking any population, or portion if it, in the mass, whatever tuberculosis exists in it will respond delicately and definitely to customs, habits, modes of life, economic and civic conditions as these affect the housing, food supply, sanitary facilities, working conditions, opportunities for recreation and employment of leisure, etc., of a community. If all these are comprehended in what we call public hygiene, then we shall find almost inevitably that where this is good and effective tuberculosis cases and deaths are relatively few, and where it is bad or ineffective they are many.

This universally noted circumstance gives us the clue as toward what direction our efforts with children must take. And, without analyzing the factors which cause tuberculosis to reflect the state of public hygiene, I would point out more explicitly where our efforts should, it seems to me, be concentrated.

Because the foundation is in existence, and much of the machinery is here, and there remain only details of execution to fashion and refine, it would appear that the schools, public, parochial and private, are the most promising media through which tuberculosis prevention is to be accomplished. There is at present much in the air in the way of plans and programmes and design; much that is sound; but how widely do performance and execution fall short of what *could* be done! Almost every child still contracts measles, and all of them frequent colds; and in most instances these maladies originate from school exposure. Add to these the number of cases of preventable whooping cough and diphtheria and tonsilitis and sore throat which are passed around in school: and we obtain an enormous case aggregate of obviable causes, which in many instances have a good deal to do with bringing out manifest tuberculosis—in neck nodes and in lungs and thence to bones and joints and even meninges; or, it may be, in thousands of patients these intercurrent infections give renewed life to tuberculous infections which were just about to die out and which, even though they caused no appreciable trouble in childhood, acquire a new stability which carries them along for years more, and even into adult life.

It was perhaps inevitable that our laudable legislation to compel attendance at school should increase the opportunities for the spread of communicable diseases and that the latter should outrun our efforts at control. But it is not so inevitable that we cannot catch up. Prevention of contagion—the means and skill to detect foci, the removal and segregation of carriers at the proper time, the keeping of weeds forever out of schoolrooms—means much more continuous and relentless attention to duty than periodic attendance on the sick; it requires much more and better medical service, much more honest and enlightened officials and much better informed public opinion than now exist in most places. To keep five hundred school children, or less, reasonably free from preventable and transmissible diseases might well require the full time of an active physician. A political hack or favorite, such as the everyday run of doctor-politician, where he exists a man, as a rule, of uncertain income in practice and of little skill in the detection of disease, cannot and does not look after ten efficiently. The time is coming when this work of school physician is going to be done by only the very best men who are specially trained for this task, who give all their time to it, and who, as a corollary, are going to be paid accordingly. This is the goal which every health body should aim at, the end that it should speed. Let us get together and work harder than ever to do away with this endless succession of preventable minor—and major—disabilities which stir up tuberculous infection in our children; it will mean big future dividends.

There must be something in our manner of life which is producing the enormous incidence of diseased teeth, hypertrophied or incompetent tonsils and adenoid growths in the nasopharynx in our children. At any rate, few reach ten years without some one or all three of these affections. Buccal and pharyngeal irritation or infection has, as is commonly observable, a peculiarly intimate effect on the cervical lymph nodes. And once we reflect that these nodes adjoin and drain the two major portals of entry of tubercle bacilli, that they are the most frequent site of clinical tuberculosis in children, that, for every case of manifest disease there are certainly several times as many infections, and that tuberculous infection within them is markedly affected by any disturbance of their normal function, we begin to realize how much healthy mouths and throats may mean in the prevention of tuberculosis. To attain maximum mass results in this respect we again have no better medium than organized prophylactic efforts in the schools; and my formula once more would be more school physicians, on full time and paid in a way to attract and demand the best talent; and, from the point of view of tuberculosis, a thorough appreciation on their part that the original excitant of tuberculosis in children is often a diseased mouth or throat.

As more physicians become familiar with the masked and obscure manifestations of tuberculosis, which are met with more frequently in children than in adults, they will prevent many later and more serious outbreaks of the disease. Many children are coming to our clinic with minor eye affections, usually phlyctenular conjunctivitis. Sometimes it antedates the appearance of tuberculous lymphadenitis or pulmonary disease, while at other times it occurs during the course of these; but in a good many it may exist alone and our experience leads us more and more to believe that an underlying tuberculosis is the etiological factor,—an opinion which is gaining wider and wider currency.

Such cases of eye disease should be treated for their tuberculosis and not merely locally for their eyes. Taken in time and put under a modified tuberculosis regimen, they respond well and escape frequently the clinical evidence of more advanced infection. They are frequent among children, and their recognition and handling as tuberculosis constitute prophylactic work of the first order. There are, besides, other children who may exhibit their infection, for a time at least, only by skin eruptions, of which several are now pretty satisfactorily determined as of tuberculous origin. Those who are taken in hand and treated for tuberculosis, and not allowed to go their way after the application of ointments and powders, will again in many cases fall out of the ranks of future consumptives.

The prevention of adult tuberculosis which quasitherapeutic institutions like the open air school, or schools adapted to the peculiar needs of delicate children, can do is incalculable: they will repay any amount of development. What children themselves assimilate from such movements as that of the Health Crusaders cannot be estimated; but the conclusion is inescapable that thousands will carry precept and practice, even though imperfectly, through childhood and into later life, and will translate into action and habit health practices which on occasion will turn the scale in favor of the continuation and permanence of the inactivity of long-standing infection.

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Abstracts of Tuberculosis ***is published at intervals as an integral part of the*** **American Review of Tuberculosis.** ***It will receive separate paging and may, if desired, be bound separately at the completion of the volume.***

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Enlightening the Public.—The basis of the modern fight against tuberculosis is enlightenment, instruction and education of the public. This is carried on mostly by pamphlets and printed rules. Usually the patients read and understood them either imperfectly or not at all. The author proved this by giving the patients verbal orders to bring in specimens of sputum and urine with the result that almost every one complied with the order. To another group of patients he handed pamphlets in which he enclosed slips on which were printed the same directions. The results were less good. The third experiment in which he printed the same directions inconspicuously on the second page of the pamphlet had the result that practically all patients failed to bring in the specimens. He therefore places little value on printed matter and tries to carry on all education and instruction verbally. Special informatory and advisory office hours were instituted at the *Fürsorgestelle.* Special lectures are given with open dis-. cussions and practical demonstrations. They are so well attended that it has become necessary to hold them in a larger hall. There will always be people who can learn from printed directions, but the great mass of the people will follow verbal instructions better.—*Von welcher Art der Aufklärung darf man den grössten Erfolg erwarten–Beschorner, Tuberculosis, October, 1920, 251.*

Interesting Things About Tuberculosis.—There is probably no condition that presents a more varied array of symptoms than incipient tuberculosis. The fact that a patient has tuberculosis does not rule out the presence of other diseases. The patient's chances for recovery depend greatly upon how early the disease is discovered and how successfully it is treated. Among the more common tuberculous manifestations are pleurisy, laryngitis, adenitis, fistula, meningitis, ostitis, arthritis, colitis, and peritonitis. At the present time the old idea prevails that the West is the only place in which one suffering from tuberculosis can recover. It is more important to live the proper life and to learn to take precautions to prevent the spread of the disease. Drugs are of little use in the treatment, though they may relieve certain symptoms. Fresh air, good food, rest and exercise properly used are of far more value than anything else yet discovered.—*Some Interesting Things About Tuberculosis, S. A. Slater, Med. Rec., January 8, 1921, xcix, 56.*

The Soul of the Consumptive.—We all know something about the physical sufferings of the consumptive, but how many of us fully realize what the consumptive suffers in mind and soul. The well-to-do consumptive suffers because he has failed to do his duty in preventing his employees from becoming infected. The rich and poor tuberculous think of saving others even when realizing that they cannot be saved themselves. They worry because they cannot provide for their family, and the conscientious ones harbor a fear that they may give the disease to others in spite of precautions. Phthisiophobia has caused and is causing more suffering to the consumptive than it is possible to imagine. People will not employ even the recovered consumptive and some are afraid to associate with him. A plea is made to let the employer do justice to his employees by periodical examinations for tuberculosis and the provision of proper sanitation for factory, workshop, and store. The worker found to be tuberculous must receive proper and timely treatment. Cities, towns and villages must see to it that there are no insanitary dwellings. An appeal for financial help and encouragement is made.—*The Soul of the Consumptive. A Plea for Justice, S. A. Knopf, N. York M. J., January 1, 1921, cxiii, 24.*

Why Tuberculosis Schemes Fail.—By tuberculosis schemes the author means only such attempts at prevention or treatment as have been sanctioned or adopted by a considerable number of leaders in the antituberculosis campaign. All these have failed because, even in the countries where all or some of them have been in operation for twenty years or more, every tenth or twelfth death is still caused by tuberculosis; because in spite of the functioning of any or all of these schemes, tuberculosis continues to drag its victims from the rank of the rich and the educated as well as from the poor and ignorant; and because, while it must be admitted that these tuberculosis schemes have reduced the tuberculosis death rate, there is very little proof that they have reduced the tuberculosis death rate any more than they have reduced the general death rate. They have simply caused the people to focus their attention on the need of cleanliness—clean air, homes, food, drink, streets, hands, mouths, bodies, barns, cattle and, perhaps, clean lives. As measures for promoting the general health of the community they have been worth while, but as tuberculosis schemes they have been failures. The reasons for the failure of all tuberculosis schemes are the overemphasis given to the value of the activities of the nonmedical antituberculosis workers, the disinclination of most physicians to join heartily in a medical campaign dominated by nonmedical functionaries, the obtuseness of even the medical officers of the tuberculosis campaigns to the importance of the following facts: (1) Aside from its specific toxic power, the most important character of the tubercle bacillus is its waxy, resistant capsule. (2) Serological tests prove that there is a family relationship between tubercle bacilli and all bacilli that possess these waxy capsules. (3) Many ordinary nonacidfast bacteria, when subjected to an unfavorable environment, develop waxy capsules, and thus become demonstrably family relations of the tubercle bacillus. This was known to be true of colon, subtilis, typhosus, mycoides and streptothrix. Measures must be devised that have for their object the securing of such special conditions of person and domicile as prevent the transformation of the digestible or innocent, "thin-skinned" forms of bacterial life into the "hard-shelled," disease producing tubercle bacilli. The theory that all disease producing germs are simply abnormal developments from forms of bacterial life that under ordinary and favorable conditions of environment are harmless or beneficial to human and other animals is formulated. The practical difficulties in connection with the carrying out of tuberculosis schemes are due to the false hypothesis on which they are based, namely, that all tubercle bacilli must of necessity have been born of other tubercle bacilli. As an argument in favor of his contentions Maher cites the history of the following cultures: Avian B, a strain of avian tubercle bacilli, that ten years ago grew entirely acidfast and only at blood temperature, now grows at room temperature and almost entirely nonacidfast. Bovine B, a strain of bovine tubercle bacilli, has a similar history. Red K, sent to Trudeau nearly forty years ago by Koch, now has chromogenic powers, grows at room temperature, is nonpathogenic and almost nonacidfast. R.R.H., an ordinary pathogenic human tubercle bacillus culture, grown for long periods on glycerine potato, first developed chromogenesis, then lost acid resistance and acquired power to grow at room temperature; it now does not cause tuberculosis and on some media loses its bacillary form and becomes coccoid. 512, acidfast bacilli, derived from bacillus subtilis, made acidfast by age and lowered temperature, subjected to the slightly stimulating but difficult environment of normal salt solution and a temperature of 37.4°, do not cause tuberculosis, when injected into guinea pigs intraperitoneally give rise in ten days to small nodules that are not fatal and that disappear in three weeks.—*How "Tuberculosis Schemes" Fail and Why, S. J. Maher, Med. Rec., December 11, 1920, xcviii, 967.*

War and Social Prophylaxis.—Official statistics of the French Ministry of the

Interior gave 83,000 as the annual average of deaths from tuberculosis, while some authorities claimed that the deaths numbered from 120,000 to 150,000 annually. The truth probably lay between these two extremes. The number of men invalided from the army through tuberculosis exceeds 110,000. During the war the Ministry of the Interior organized hospitals called *stations sanitaires* for the treatment of tuberculous soldiers coming from the special army hospitals known as *hôpitaux sanitaires*. The patients were admitted to the *stations sanitaires* prior to being invalided out of the army; and during their stay, the length of which varied, they received sanatorium treatment and education in prophylaxis. On leaving the *stations sanitaires* and returning to their homes, these invalided soldiers were dealt with by a departmental Committee for the Relief of Tuberculous Discharged Soldiers. These district committees, although the result of private, independent initiative, were organized on a uniform plan laid down by the government, and supported and assisted by government authority and subsidies. The activities extended throughout the country, working through the intermediary of delegates or visiting nurses and furnished food, medicines, prophylactic materials and beds to those in need of them. The activities of the district committees were coördinated and facilitated by a National Committee for the Relief of Tuberculous Discharged Soldiers. The achievements of these committees have been considerable. They enable France to undertake an antituberculosis campaign based on sound principles and to provide tuberculous soldiers with adequate assistance and relief. The antituberculosis programme includes the organization of dispensaries, sanatoria, and special hospitals or special sections of hospitals. The dispensary constitutes the actual centre of all antituberculosis organization. The patient is examined there and classified from the medical and the social point of view. The visiting nurse has the opportunity of discovering other centres of infection and of reporting them to the dispensary, which sends the sick either to the sanatorium or hospital. The dispensary is notified when patients are discharged, and undertakes their further care. The sanatoria are reserved for curable cases. They will be more efficient when completed by a social organization of the nature of an employment bureau providing work suitable to this special class of invalid. The tuberculosis hospital is reserved for those cases in which there can be no hope either of a cure or of economic recuperation through work. The isolation of tuberculous cases in the hospitals is considered an imperative duty. The isolation can be carried out in various ways, either by arranging special wards, sections or annexes in the general hospitals. The programme includes the boarding out of children through such societies as the *Oeuvre Grancher*, and an educational propaganda like that carried on formerly by the *Société de Préservation contre la Tuberculose* and today by the Rockefeller Commission and the *Comité National D'Assistance aux Anciens Militaires Tuberculeux*. This programme is in full execution: 200 dispensaries have been established; schools for visiting nurses have been opened; 11 new sanatoria have been organized. The *hôpitaux sanitaires* and *stations sanitaires* will become civilian sanatoria. The tuberculous war invalids, like all disabled and invalided soldiers, are on much the same footing as the rest of the civilian population, and are entitled to the relief and assistance of the institutions established by the civilian authorities. As regards the social prophylaxis of the disease, the antituberculosis organization represents only one link in the chain with which the disease must be hemmed in. It cannot attack tuberculosis at its sources. In order to do that it will be necessary to include the institution of appropriate protective measures, radical changes in housing conditions, a campaign against alcoholism, and the education of children in matters of health.—*The War and the Social Prophylaxis of Tuberculosis, L. Bernard, Internat. J. Pub. Health, November, 1920, i, 281.*

Campaign Against Tuberculosis in Wales.—The North Wales Sanatorium and the South Wales Sanatorium provide 538 beds. Wales and Monmouthshire are divided into 14 dispensary areas, each with a tuberculosis physician. In each area there are a number of visiting stations at which the patients are seen and examined once a week or once in a fortnight. Beds are provided in certain hospitals, at which both pulmonary and nonpulmonary cases are treated. These hospitals are entirely distinct from the sanatoria. Sanatoria have been founded at various centres. The North Wales Sanatorium is near Denbigh, and is for women; the South Wales Sanatorium, Talgarth, is for men. The West Wales Sanatorium at Llanybyther is for women and children; the Penhesgym Sanatorium, Anglesea, is reserved for girls. A farm colony with 50 beds for discharged service men is conducted in connection with the South Wales Sanatorium. An educational campaign is being carried on throughout Wales by means of lectures in all the elementary and secondary schools. The Council of the Association for Prevention, Treatment and Abolition of Tuberculosis has adopted the principle whereby the Chief Medical Officer becomes the Professor of Tuberculosis at the Welsh National Medical School. A description of the Sanatoria mentioned follows.—*The Campaign Against Tuberculosis in Wales, D. W. Evans, Brit. J. Tuberc., October, 1920, xlv, 166.*

Tuberculosis in Austria.—The Austrian Government has issued, through Dr. S. Rosenfeld, a report on the mortality from tuberculosis during and since the war within the territories of the present republic. In Vienna, 2725 women died of tuberculosis in 1912, and the figure had fallen to 2635 in 1914. There was an increase to 3004 in the first year of the war. The quotas of the four following years are 3543; 4469; 4729; 5018. In England the war was associated with a slight but sensible increase of mortality from tuberculosis among women, which has been attributed to the introduction of large numbers of women to factory work with consequent overstrain. Whereas in England and Wales the rates at most ages for 1919 fell to prewar levels, the Viennese figures for 1919, especially for the ages between thirty five and sixty-five, are worse than those of any former year. The inference drawn by Rosenfeld is that the prime factor has been the progressive deterioration of nutrition, due to economic consequences of the war. The war has thus afforded an experimental proof that the decline in the death rate from tuberculosis prior to it was not a consequence of measures of segregation and of prevention of infection, but was dependent upon a general amelioration of economic conditions leading to the attainment of a better standard of nutrition. There is a lack of agreement respecting the fundamentals of etiology amongst competent students of the tuberculosis question. The dispute is not of mere theoretical interest; its settlement would gravely affect administration. The most hopeful feature is the better temper in which the discussion is conducted. The value of different lines of research is more generally realized, and this will perhaps lead to the discovery of great truths.—*Tuberculosis in Austria, Leading Article, Brit. M. J., November 27, 1920, 829.*

Causes of Death in United States Registration Area, 1919.—The Census Bureau's annual bulletin on mortality statistics for the registration area in Continental U. S. shows 1,096,436 deaths as having occurred in 1919. This represents a rate of 12.9 per 1000 population and is the lowest rate recorded in any year since the establishment of the registration area. The rate for 1919 is in striking contrast with the unusually high rate for 1918, the year of the pandemic of influenza, which was 18 per 1000. There was therefore a drop of 5.1 per 1000. The death registration area comprised 33 states, the District of Columbia, and 18 registration cities in nonregistration states, with a total estimated population of 85,147,822 or 81.1 per cent of the estimated population of the U. S. Of the 1,096,436 deaths, organic disease of the heart was the most frequent cause of death, the number being 111,579. Tuberculosis (all forms) was next frequent, with 106,985 deaths, or 125.6 per 100,000 population, or 9.8 per cent of the total. There were 94,772 deaths from tuberculosis of the lungs, or 111.3 per 100,000 population; 5,175 deaths from tuberculous meningitis, or 6.1 per 100,000 population, and 7038 deaths from other forms of tuberculosis.—*Principal Causes of Death in United States Registration Area, 1919, Pub. Health Rep., xxxv, November 19, 1920, 2787.*

Public Health Service Forced to Transfer Tuberculosis Patients to the East.—All the hospitals and contract hospitals of the United States Public Health Service in the semi-arid southwest are already crowded with tuberculosis patients and the influx of others from the eastern states continues so great that the Public Health Service has been forced to transfer patients from Tucson, Ariz., and other western hospitals to sanatoriums near Asheville, N. C., and elsewhere in the east. Many ill-advised patients have of late thronged to Tucson, unmindful of the fact that every hospital bed in that place is filled and every hotel and boarding house overcrowded. More than 500 tuberculosis subjects in Tucson are unable to find entrance to a sanatorium. Other towns in the southwest report similar conditions. Surgeon General Cumming again renews his warning against tuberculosis patients leaving sections where the government is able and willing to care for them and going to the southwest on their own initiative.—*Bull. Pub. Health Service, January, 1921.*

Deaths and Death Rates from Pulmonary Tuberculosis in New York City and State.—The following tables, showing the deaths and death rates from pulmonary tuberculosis for New York City and State, for October and November, during the years 1913 to 1920, inclusive, are taken from the *Monthly Vital Statistics Review, New York State Department of Health, December, 1920, and January, 1921, New Series, vol. i, nos. 10 and 11.*

Pulmonary tuberculosis: Deaths and death rates, New York State and large subdivisions, October, 1913, to 1920*

MONTH	YEAR	NEW YORK STATE		NEW YORK CITY		REST OF STATE							
						Total		Urban		Rural		Institutional Districts	
		Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
October average	1913–17	1,057	123.1	647	139.3	410	104.0	203	106.1	207	102.0		
October	1913	1,040	125.8	604	136.8	436	113.4	224	119.7	212	108.0		
October	1914	1,021	121.2	646	143.0	375	96.6	205	107.3	170	86.4		
October	1915	1,100	128.0	692	149.0	408	103.5	188	98.3	220	108.4		
October	1916	1,034	118.5	633	133.3	401	100.8	197	101.7	204	99.9		
October	1917	1,089	122.2	662	136.2	427	106.0	199	101.0	228	110.3		
October	1918	1,520	168.0	851	171.0	669	164.1	287	143.0	316	152.1	66	
October	1919	813	88.0	481	94.5	332	80.5	144	70.5	159	76.1	29	
October	1920	726	77.5	408	78.4	318	76.2	129	62.4	155	73.7	34	

* Deaths per 100,000 population per annum.

Pulmonary tuberculosis: Deaths and death rates, New York State and large subdivisions, November, 1913, to 1920*

MONTH	YEAR	NEW YORK STATE		NEW YORK CITY		REST OF STATE							
						Total		Urban		Rural		Institutional Districts	
		Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
November average	1913–17	1,066	128.2	670	149.1	396	103.8	201	108.6	195	99.3		
November	1913	1,060	132.6	642	150.2	418	112.3	199	109.9	219	115.3		
November	1914	1,034	126.8	690	157.8	344	91.5	177	95.7	167	87.7		
November	1915	1,092	131.4	673	149.7	419	109.9	227	122.7	192	97.8		
November	1916	1,071	126.8	686	149.3	385	100.0	201	107.2	184	93.1		
November	1917	1,074	124.6	659	140.1	415	106.5	202	106.0	213	106.5		
November	1918	1,230	140.5	727	151.1	503	127.6	210	108.2	241	119.8	52	
November	1919	784	88.0	452	91.8	332	83.2	116	58.8	171	84.8	45	
November	1920	756	83.3	440	87.4	316	78.3	142	71.0	147	72.2	27	

* Deaths per 100,000 population per annum.

Low Tuberculosis Death Rate for November, 1920.—The death rate during November continued exceedingly low, although a very slight increase is in evidence as compared with October. The general health situation over the country remains favorable. The outstanding feature in the health record of the month is the remarkably low rate for tuberculosis, namely, 109.7 per 100,000 exposed. This marks a new minimum for this disease in the experience of the Industrial Department of this Company (Metropolitan Life Insurance Co.). The lowest figure for any prior month was that for September of this year—111.3 per 100,000.—*Statistical Bulletin, Metropolitan Life Insurance Co., December, 1920, vol. i, no. 12, p. 8.*

Vital Statistics for the Year 1920 in New York City.—The year just closed has established a record as the healthiest year that the city has ever experienced at any time in its history. There were 73.249 deaths reported and a death rate of 11.93 per 1000 of the population, as compared with 74,433 deaths and a rate of 12.39 for the year 1919—a decrease in the absolute number of deaths of 1184, and in the death rate of 0.46 of a point, which is equivalent to a saving of 2824 lives, taking into consideration the increase in the population during the year 1920, as compared with 1919. Three prominent features of the year's mortality from individual causes stand out as indicative of improved health conditions. First and foremost, the mortality from pulmonary tuberculosis and other forms of tuberculosis. During the year, there were 6164 deaths reported from tuberculosis of the lungs, with a death rate of 1 per 1000 of the population, as compared with 7395 deaths and a rate of 1.23 in 1919—a decrease of 1231 deaths and 0.23 of a point in the rate, which, if the increase in the population be taken into consideration, means a saving of 1412 lives. From other forms of tuberculosis, there were 970 deaths reported during the year, as compared with 1103 deaths in 1919—a decrease of 133 deaths, equivalent to a relative decrease of 246 deaths, so that all told the mortality from tuberculosis showed a decrease of 1657 deaths. The most important factors in causing this decreased mortality from tuberculosis are three in number: First.—The increased amount of money received by each family as wages, with the result that a greater quantity of nutritious food was obtainable by people prone to tuberculosis. Second.—The greater opportunity for relaxation, open-air exercises, and social enjoyment. Third.—The increase in the spread of knowledge of this cause of death and sickness. This decrease in the mortality from tuberculosis is by no means a local manifestation, as the same improvement in the death rate from this cause is noted in all of the large cities of the country.—*Weekly Bull., Dept. of Health, N. Y. City, January 8, 1921, x, 11.*

Statistics of Tuberculosis Institutions.—At the first meeting of the Society of Superintendents of Tuberculosis Institutions, a committee of three was formed to inquire into the possibilities of the coördination of statistics of such institutions. The following article is based on this inquiry. From the results the author finds that there is a great need for coördination. He has attempted to give a basis for the coördination of statistics of tuberculosis institutions. There must be secured uniformity in clinical classification, in describing immediate results and after-results of treatment, in the registration of all cases treated, and a uniform case sheet and method of symbolic representation of physical signs. There are four main factors which have an influence on prognosis, and therefore on classification. All previous methods were based on one to three of these factors and were thus defective in the omission of one or more factors. The suggestion offered is to classify all four factors in degree independent of each other. (1) The extent of the lesion: L_1 = involvement of one lobe or less. L_2 = involvement of 1–2 lobes. L_3 = involvement of 2–3 or more lobes. L_4 = multiple lesions (e.g., larynx or intestines involved). (2) The type of the lesion: The four stages of chronic lung tubercle are: (i) Infiltration = T_1, fine crepitations and slight dulness. (ii) Consolidation = T_2, dulness extensive with bronchial breathing. (iii) Excavation = T_3, vomica formation or extensive breaking down. (iv) Fibrosis = T_4, fibrous changes. (3) Systemic effect: Pyrexia, tachycardia, night sweats, emaciation, anemia, nervous symptoms, hemoptysis, and anorexia. The grades are: S, no systemic effects present. S_1, where some of the systemic effects are present but none severe. S_2, where all eight are present or one very severe. (4) Sputum as to presence of tubercle bacilli: Four degrees T. B. 0, T.B. +1, T.B. +2, T.B. +3. The returns from 33 sanatoriums disclosed 24 different methods of describing immediate results. The following terms should be used in regard to systemic effects. MI = Systemic effects disappeared. I = Systemic effects lessened. I S Q = Systemic effects unaffected. W = Systemic effects worse. D = died. The condition of the sputum as to tubercle bacilli must be reckoned with. (1) Bacilli absent on admission and on discharge = T.B. 0 K. (2) Present on admission and on discharge = T.B. +K. (3) Present on admission and absent on discharge = T.B. + 0. (4) Absent on admission and present on discharge = T.B. 0 +. About half of the sanatoriums kept statistics of late results. These are more important than the immediate results. Therefore such statistics should be compulsory. The usual classification used is full work, partial work, no work, died, lost sight of. As to uniform case sheets, the author had sent to him the case sheets of over 30 sanatoriums and scarcely any one was the same as any other. Some were overcrowded with details; others had too few. Those that give state on admission in full details along with a summary of the state on discharge as compared with the state on admission are to be preferred. A standard case sheet is included in the report. All sanatoriums should have a bound register giving the main facts of each case. An attempt should be made to get unanimity in the symbolic representations of physical signs. A scheme for the symbols to be used is included in the report. —*Coördination of Statistics of Tuberculosis Institutions, N. Robertson, Tubercle, December*, 1920, *ii*, 97.

Etiologic Factors in Pulmonary Tuberculosis.—That the tubercle bacillus is the direct cause is indisputable, but from this fact as a starting point the path deviates and leads to an interminable maze of individual opinion. The important major premise that all pulmonary tuberculosis has its origin in infancy and childhood, and the minor premise that the human type of bacillus is responsible for the bulk of the infections, must, in the light of past experiment and present knowledge, be accepted. Tuberculous adenitis, the precursor of adult pulmonary tuberculosis, is the primary infection. Adult pulmonary tuberculosis, or the secondary manifestation of the tuberculous infection, is in the nature of a metastatic process. There are two essential requisites for a beginning pulmonary tuberculosis: the primary infection of childhood, plus the fertile soil, the lowered resistance, the predisposition. The occurrence of intrauterine infection, the transmission of the disease from the father or the mother through heredity and the occurrence of congenital tuberculosis have not been proved. The child of a father or mother, who is actively tuberculous at the time of its birth, is handicapped and influenced in two ways. It is deprived of an eugenic start in life, and is subjected from its earliest infancy to infection through direct contact, especially if the affected parent be the mother. Any condition or disease which impairs, locally and permanently, the respiratory tract, especially the lung or pleura, is a predisposing factor to pulmonary tuberculosis. Primary pleurisy with effusion is synonymous with tuberculous pleuritis. The focus of infection in such pleurisies may be located in the parietal pleura, but in the vast majority of cases it is of pulmonary origin. Dry pleurisy is of tuberculous origin in a heavy percentage of cases, provided it be a true pleurisy. After examining and following up more than 500 cases of measles, the conclusion was reached that this disease deserves no important place among the predisposing factors. Of the 500 cases examined, only one gave conclusive proof of reactivation directly attributable to measles infection. A study made during the influenza epidemic of 1919 on more than 30 cases of quiescent and healed pulmonary tuberculosis revealed reactivation of 13 cases directly attributable to influenza, i.e., over 40 per cent. The importance of the various occupations has been generally overestimated. The following practical points should be observed: (1) An infant of an actively tuberculous parent should be guarded as early and as thoroughly as possible, even if it entails the separation of the infant from the parent. (2) At the age of four or five years, all suspected glandular patients should be carefully examined and checked with X-ray examinations and Pirquet tests. If a positive diagnosis is arrived at, such a child must be treated sanely but vigorously. It is as essential to enforce absolute rest on a tuberculous infant and child, with an active lesion, as it is in the adult. The exact mechanism of immunity is far from being clear, but we know that rest is the greatest synergist of passive immunization. Ten days to two weeks in the average case is probably sufficient. (3) All school children at the age of seven years, or at least all suspicious cases should be given Pirquet tests and, if positive, a thorough course of protective treatment. (4) Children who have had glandular infections should be closely watched and followed into adult life. As adults they should be dealt with frankly and warned that pernicious habits such as excessive smoking, excessive venery, venereal disease, etc., may light up the smoldering ember and result in an active pulmonary tuberculosis.—*A Consideration of Etiologic Factors in Pulmonary Tuberculosis, R. S. Berghoff, Annals of Med., July, 1920, i, 276.*

Relation of Contact to Development of Tuberculosis.—Experimental evidence has shown that such objects as gauze used to cover the mouth when coughing, pillow cases used twenty-four hours, patients' hands, spoons used by patients, magazine covers picked up indiscriminately from the wards, and door-knobs frequently handled by patients are contaminated with living, virulent tubercle bacilli. Patients with open tuberculosis frequently emit infectious particles when coughing. If these particles are collected 15 inches from the mouth of the patients, 35 per cent of a group of guinea pigs can be infected; if collected at a distance of 6 inches, the percentage increases to 75 per cent. Such particles, no doubt, are inhaled by persons in close proximity to the patients. The saliva in open cases of tuberculosis usually contains living tubercle bacilli. The sedimented urine in twenty open pulmonary tuberculosis cases negative for genitourinary tuberculosis failed to infect any of the twenty inoculated guinea pigs. Out of 240 nurses employed at the Cincinnati Tuberculosis Sanatorium, only three developed tuberculosis, and one diagnosed as tuberculous after working at the sanatorium for two years gave a history of previous infection.

Aside from the mere presence of the organism in the body, other factors are necessary for the development of clinical tuberculosis. What the factors are has not as yet been clearly shown. In all probability there must be a lowering of the individual resisting power; whether this is congenital or acquired, whether purely local or constitutional, resulting from pathologic states or physical abnormalities, is still a question. At all events, we may safely assume that the elimination of clinical tuberculosis from adults will largely depend on the establishment of such living conditions as will keep up to normal those powers of individual resistance.—*Relation of Contact with Tubercle Bacillus to Development of Tuberculosis in Adults, J. B. Rogers, J. Am. M. Ass., December 18, 1920, lxxv, 1690.*

Is Tuberculosis Contagious?—Ghon and Hamburger have shown in numerous autopsies that the human bacillus enters the system through the lung. In the larger cities Pirquet tests, X-ray and physical examinations, show that 90 per cent of children under 14 years are infected; in rural communities, it may be as low as 25 per cent. It is believed that these infected people cannot receive a secondary infection. The logical conclusion must be that tuberculosis is primarily a disease of the lymph nodes, a disease of childhood, that once a person becomes infected he will remain so as long as he lives, to give tangible expression of such infection by the invasion of the lung if conditions occur which will bring the bacilli out of the lymphatics into the blood stream. Laennec was one of the first to announce that tuberculosis of the lung is not contagious from man to man, that the danger of contagion is largely with children. Wilson Fox found but two instances of married couples infecting each other in over 27 years experience. Weber, West and Osler found a similar paucity of instances of contagion between man and wife and between the invalid and the attending nurse. Tuberculosis is positively contagious to every child, and generally produces an infection. In the tuberculosis clinics of Jersey City no Pirquet negative or X-ray negative case in the adult, whether nurse, attendant, or physician working in tuberculosis institutions, has ever come down with an active process in the lung in the author's experience. All of the attendants are given careful examinations before employment. A number of them show infection; many of them show healed lesions; a large percentage are in a position to "explode" on provocation. These are the ones which the general profession say "caught it."—*Is Tuberculosis Contagious? G. K. Dickinson, Med. Rec., December 4, 1920, xcviii, 943.*

Diseased Tonsils and Pulmonary Tuberculosis.—In a series of cases referred for nose and throat examination during the past six years, it was observed that practically every case gave a history of recurrent inflammation of the tonsils, at some time or other, and upon examination the crypts were found to be filled with deposits of thickened pus. Some cases gave no history of a tonsillar inflammation, but the tonsils were found similarly diseased. In the army the author had the opportunity of doing practically all the nose and throat work for approximately 28,000 men and found not a single case of tuberculous infection which did not give a history of tonsillar involvement associated with it. Men sent into the hospital with symptoms of an incipient pulmonary tuberculosis were referred for a nose and throat examination; these consistently revealed diseased tonsils. In a number of cases tonsillectomy was advised and performed as an adjunct to the treatment of the pulmonary condition. In the larger proportion of cases thus treated, beneficial results were obtained. Men were frequently returned to active duty, who otherwise would have been sent to the rear. The removal of the tonsils in pulmonary tuberculosis is advanced as a theory only, unsustained as yet by laboratory and clinical findings. It is maintained, however, that there is a distinct relationship between tonsils and pulmonary tuberculosis, and that markedly beneficial results are obtained by tonsillectomy when performed during the initial stage of the disease.—*The Relationship Between Diseased Tonsils and Pulmonary Tuberculosis, W. L. Rhodes, N. York M. J., December 4, 1920, cxii, 902.*

Infants of Tuberculous Mothers.—Bernard and Debré conclude from 123 cases that the infant of a tuberculous mother does not inevitably contract the disease at once; some were saved even after from eight days to three months of contact with the tuberculous mother. None of the infants failed to contract the disease with over six months of contact. The contaminated infants almost all died within a month after being taken from the mother, even those that seemed healthy at first. Hence if the infant taken from a tuberculous mother outlives the second month, there is reason to hope that it will survive, but only a series of negative tuberculin skin reactions will confirm that the child is sound. They commend boarding out these infants in country families. Only 18 children survived of the 58 who were cared for by mothers with bacilli in the sputum, but 57 survived from the 65 mothers with "closed" tuberculosis.—*Les modes d'infection et les modes de préservation de la tuberculose chez les enfants au premier âge, L. Bernard & R. Debré, Bull. d. l'Acad. d. Med., October 5, 1920, lxxxiv, 86.*

Pulmonary Tuberculosis in Childhood.—Ghon's primary focus in the lungs with secondary infection in the bronchial glands afforded a sure anatomic pathological basis for clinical investigation. The tendency towards healing of the usually small primary tuberculous infection explains the positive tuberculin reaction in spite of negative lung findings. The value of the X-ray in the recognition of latent hilum glands and lung foci especially in children cannot be doubted. The key to the understanding of the conflicting views in regard to tuberculin therapy is the lack of a uniform classification. Theoretically it is possible to realize the structural processes in the diseased tissues and to ascertain the applicability of a specific therapy by means of the diagnostic biologic reaction with Deycke-Much's partial antigens. The clinical classification of pulmonary tuberculosis according to anatomic pathologic processes is indispensable for the indication and prognosis of the pneumothorax therapy. Its success and failure stand in close relation to the anatomic character of the disease. The present collapse therapy lacks objectivity and does not consider the anatomic pathology. The occurrence of pleural exudation during pneumothorax therapy has caused reluctance in employing this treatment. The pneumothorax exudate is not always undesirable, as it causes increased compression of the lung and has a favorable serological immunizing influence. The frequency of its occurrence stands in direct relation to the degree of involvement of the pleura. But if the exudate becomes purulent this signifies a serious progressing tuberculosis. In that case the pleura reacts to the increased stimulus of the pneumothorax with greater activity and exacerbation. The differentiation of the shadows in roentgenograms of the lung caused many difficulties at first. A collection of 33 characteristic roentgen ray pictures of pulmonary tuberculosis in childhood with the clinical histories is incorporated in the book. They prove how conclusive the X-ray picture is for an early diagnosis. The sooner the early stages are recognized in childhood and the sooner treatment in institutions is possible, the sooner tuberculosis as a public plague will be controlled. Whereas in the adult the appearance of a spontaneous pneumothorax is connected with a cavernous process, there appears to be a different etiology in the young child and infant. Langstein and Ypo state that pneumothorax occurs more frequently in the young child than is commonly believed. The most frequent causes are small nontuberculosis abscesses with rupture into the pleural cavity and following empyema. In the 100 cases of tuberculosis observed by Harms since 1912, there were 2 cases of spontaneous pneumothorax diagnosed and confirmed by autopsy. There is also a paucity of statistics on artificial pneumothorax. While the importance of tuberculosis in childhood is recognized by science, daily practice has not yet conceived and utilized it. The diagnostic difficulties lie in the absence of sputum, in remissions lasting months to years, in the afebrile course of even active tuberculosis, and in the possibility of gain in weight in spite of progressing tuberculosis. The tuberculin reaction while indicating the infection proves nothing about the activity or inactivity of the process, except in earliest infancy. The fight for early diagnosis and treatment must be carried on with the aid of the school physicians infant welfare and welfare stations for the tuberculous. Systematic pneumothorax treatment was first used in the Strassburg clinic. Of the 10 cases reported, 6 were tuberculous, 4 chronic bronchiectasis. In 4 of the 6 cases the temperature became normal and the general condition improved, the longest period of observation being nine months. Pneumothorax treatment will show good results in childhood as soon as it is understood that the course of childhood tuberculosis in general is less favorable. Of the 100 cases observed by Harms in the welfare station or city hospital in Mannheim, Germany, the sputum was positive in 65. In the others positive diagnosis was made on physical and X-ray findings. Of the 65 open cases two-thirds were girls. This relative frequency in girls has been observed by others without an adequate explanation so far. Twenty-one cases were selected for pneumothorax treatment because the process was unilateral. The most frequent forms besides the miliary, were the infiltrating, the nodular and the pneumonic, all originating in the hilum region. The prognosis depends on the predominance of fibrous or exudative changes. Any form may be accompanied by cavity formation. The therapeutic effect of pneumothorax lies in the abatement of toxic symptoms and improvement of the general condition. The author's 160 observations make him consider pneumothorax a marked progress in the therapy of advanced cases. Forty-six case histories with roentgen photographs before and after pneumothorax treatment are incorporated in the book. The following rules for pneumothorax treatment in childhood are formulated: (1) The symptomatic effect is the same in adults and in children. (2) Treatment must be started earlier in children because they give a less favorable prognosis. (3) The latter, like in the adult, is dependent not only on the extent, but on the anatomic pathologic character of the disease. The fibrotic are the most favorable, the pneumonic ulcerative processes the least favorable. (4) In the fibrotic process clinical and anatomical cure may be expected, in the ulcerative only symptomatic success. (5) The duration of the treatment also depends on the anatomic basis of the disease; benign processes may heal in a period of one to two years. Gradual expansion of the lung must be watched with the X-ray. Ulcerative processes must remain under compression for several years, depending on the extent. (6) Too early expansion of the diseased lung must be avoided. (7) Serous and purulent exudates are unfavorable complications of pneumothorax treatment in the more malignant forms. (8) There are no technical difficulties peculiar to childhood, but in unmanageable children a short anesthetic may be necessary during the filling.—*Beiträge zur Lungentuberkulose im Kindesalter.* (*Die kindliche Lungentuberkulose im Röntgenbilde, Klare. Die Pneumothoraxtherapie der kindlichen Lungentuberkulose, Harms*), *Leipzig, Verlag von Curt Kabitzsch, 1920.*

Chronic Gas Poisoning and Pulmonary Tuberculosis.—The cases reported were studied by the author in United States General Hospital No. 21 (Denver), and as medical consultant to the United States Public Health Service, Duluth. The patients were men from 18 to 40 years, physically fit, who had not had influenza, pneumonia, typhoid fever or any of the acute exanthemata and whose past medical history was negative as to tuberculosis. The various kinds of gases used in the war were mustard gas, phosgene and the chlorine gases. Primarily they produce congestion, edema, ulceration and later secondary infection of the skin and all the mucous membranes with which they come in contact. The greatest damage is done to the respiratory tract. Here they produce congestion, edema, and ulceration of the bronchial mucous membrane and the inflammation spreads to the surrounding tissue, the parenchyma and the supporting framework of the lung. Sloughing and hemorrhages may occur. If the gassing has not been severe enough to cause death by asphyxiation and cardiac failure, nature begins to repair and scar tissue is formed. This condition makes a very fertile field for the growth of the tubercle bacillus and the gas as a poisonous product breaks down immunity in a sufficient degree to allow the lighting up of any old foci that may have been present. The chronic symptoms of gas poisoning do not always depend upon the severity of the poisoning. The symptoms in the order of their frequency are shortness of breath, especially on slight exertion or paroxysmal in character, weakness and early fatigue, cough, with or without expectoration, paroxysmal, occurring at various times during the day or night, pain in various parts of the chest, nausea and vomiting, poor appetite, epigastric pain after meals, constipation or diarrhea, loss of weight, hoarseness which may be intermittent, tachycardia, which may be paroxysmal, easily irritated eyes, tendency to catch cold easily, profuse perspiration and pleurisy. The writer has recently diagnosed a number of cases of tuberculosis two years after the gassing. These individuals have been examined at various times in the past two years, and heretofore a diagnosis of tuberculosis had not been made. This shows the baneful effect of the gas and it shows that it has taken two years for the old lesion to become reactivated or a new infection to become implanted. The physical examination of moderately severe cases of gas poisoning may reveal the following: diminished expansion, rarely of the entire chest, most frequently of the bases, one or both, more often the right, less frequently the upper regions; tactile fremitus increased;

depressions above and below the clavicles; respiration shallow; impaired resonance; percussion normal or even hyperresonant; inspiration rough, harsh and sometimes of the cogwheel type. In some expiration is prolonged. Over the bronchial areas the breathing is almost tubular. The râles are scattered, but are more prominent in the middle of the chest; they are of every character, come and go, and usually clear up on coughing. When the patient expires, coughs and inspires, the râles do not come at the beginning of inspiration as the tuberculosis râle does, but later during and extend through inspiration. They resemble sibilant and sonorous râles. The underlying pathological condition consists of a true inflammation of the bronchi, with some old peribronchial induration that is contracting the bronchus from the outside and infiltrating the interstitial tissue of the lung. There is also a turgescence of the mucous membrane. The pulse is usually rapid, 80 to 100. Blood pressure is normal or lowered. Stereoplates show around the bronchi and vessels more or less pronounced haziness extending far out into the lung substance. The differential diagnosis between pulmonary tuberculosis and chronic gas poisoning of the lungs is often extremely difficult. As time goes on more and more of these cases, in which a definite etiology of gas can be proved, will be found.—*The Relation of Chronic Gas Poisoning (Warfare) of the Lungs to Pulmonary Tuberculosis, F. W. Spicer, Minn. Med., December, 1920, iii, 573.*

Influenza and Tuberculosis. — The much-vexed questions of the effect of influenza on the incidence of tuberculosis and its effect upon frank, active cases, are considered, numerous authorities in this country and Europe being cited. According to Fishberg tuberculous patients have shown a relative insusceptibility to influenza, and when acquired the latter failed to hasten the progress of the tuberculosis. Amberson and Peters have taken exception to this, emphasizing the great variability in incidence of influenza among comparable, supposedly normal groups. They grant that no increase in tuberculosis mortality has occurred in recent months, but believe, like Leichtenstern in 1890, that many severe cases of tuberculosis were terminated rapidly during the height of the 1918 and 1920 epidemics, with a corresponding subsequent lull, while new cases came on. Debré and Jacquet believe that on the whole tuberculous individuals were less heavily attacked than nontuberculous groups, but abandon the common explanations that this immunity was due either to the better hygienic surroundings and prompt care of the tuberculous patient, or to a true immunity against acute respiratory diseases conferred by the chronic process. They believe that the acute process does not seriously influence an open case of tuberculosis, but curiously enough may flare up a previously dormant one. Armstrong in Framingham believed in a relative protection for the tuberculous, either because they were better educated in hygiene, or because the preëxisting infection was responsible for an actual defense against new invaders. On the other hand he too found a lighting up of hitherto unrecognized cases. W. T. Vaughan in his own experience finds that in a moderately large number of cases a preëxisting tuberculosis was tremendously fired by an attack of influenza, the latter apparently being like measles, one of the diseases of anergy. His conclusions on the subject are as follows: Great variation in the interaction of influenza and tuberculosis must be expected, because of the many stages at which the tuberculous may be attacked, because of the altered mode of living of known consumptives, and because of the protected life of most of them. Phthisical patients as a group are relatively insusceptible to influenza infection. This may be due to the tuberculous process itself or to some extrinsic but closely related cause. But many individuals with pulmonary tuberculosis do get influenza, and the disease having been contracted in many cases hastens the fatal termination of the tuberculous process. It may be that this phthisical exacerbation occurs more frequently in individuals with latent tuberculosis, individuals who are not at the same time mobilizing their protective antibodies.—*Influenza and Tuberculosis, Editorial, J. Lab. & Clin. Med., November 1920, vi, 105.*

Pregnancy in Tuberculosis.—Tuberculosis in itself does not disqualify the male or female for reproduction. The experience of the human race proves this. Tuberculosis has prevailed among civilized people as long as there are records of man's activity on earth. It was much more prevalent in the older civilizations than in our own. If it disqualified men and women for reproduction, the human family would have become extinct long ago. Occasionally the female becomes pregnant when the disease is advanced, and now and then a male who has extensive tuberculosis is capable of procreating, especially if the disease has been arrested even temporarily. Ordinarily the children of tuberculous parents come into the world well formed, well developed, and in good health and, if protected against implantation, grow up into strong adults.

Pregnancy does not shorten the life of a tuberculous woman. On the contrary, if proper advantage is taken of it, it may prolong life. In the organism of a pregnant being all functions are first for the welfare of the new being, and next for the welfare of the parent. So intense, however, is the interest of the organism in the new being that with proper direction, it can be made to work also for the parent. In pregnancy desire for food and capacity to change food into tissue increases, especially after the third month. and, if in health, the pregnant woman not only makes the tissues for the new being, but stores up some for herself. When a pregnant woman has tuberculosis her desire for food increases. but her capacity for changing the food into tissue may have been lessened by the injury which has been done to her lymphatic system, to her lungs and alimentary canal. By putting her organism in the best condition possible for physiological action, by putting her body at rest so as to cut down the consumption of energy to the lowest point, and by selecting her food so as to get the largest return in healthy blood cells with the smallest consumption of energy in making them, her capacity for changing food into tissue can be brought up to her desire for food, and thus make her pregnancy a means of recovery for her, In itself, pregnancy does not hasten the progress of tuberculosis. This has been proved by experiments on animals. Pregnant animals which have been injected with tubercle bacilli have lived as long as non-pregnant ones. The only handicap which comes to a pregnant being in its struggle against tuberculosis is in the injury which the disease may have done to that part of the organism which has to do with nutrition and this can be overcome with treatment. The innocuous influence of pregnancy on tuberculosis is strikingly shown by the mortality statistics from tuberculosis in all civilized communities at the present day. The death rate from tuberculosis is very much lower in the female than in the male, and yet the child bearing years have the highest mortality from the disease. There may be accidents of pregnancy which can bring about recrudescence in dormant tuberculosis. It occasionally happens that within six or eight weeks after parturition a tuberculous process which has been quiescent for a long time becomes active and runs a virulent course. The author is convinced that the recrudescence is due most frequently to mild sepsis, occasionally to subinvolution. and now and then to the giving of ether. These are accidents which can be avoided. It might be well to mitigate the severity of labor in tuberculous women by the use of gas and oxygen or a little chloroform, which do not seem to be contraindicated in tuberculosis. Contraceptive practices. except continence, and abortion in all probability are more conducive to activity in tuberculosis than pregnancy. Metabolism plays an important rôle in the fight against tuberculosis. and the mental distress and irritation, which accompany and follow unnatural contraceptive acts seriously disturb metabolism. Abortions are a much more fruitful cause of recrudescence than parturition. There are reasons why individuals who are advanced in tuberculosis or who have the disease in an active form should not get married, but the reasons are not predicated upon procreation or upon pregnancy. A person who has been seriously injured by tuberculosis, when restored to good physical health, must live a careful, easy life to remain well. The worry and hardships of married life. which may come to people of moderate means are conducive to recrudescence and activity as long as living tubercle bacilli remain in the body. The advisability of marriage for tuberculous individuals depends upon whether the disease is dormant or active, how far it has progressed, whether the conditions of life in the married state will be more conducive to physical well-being and to happiness than in the single state and a willingness of the healthy party to the marriage contract to enter upon the contract with a full and complete knowledge of the condition of the tuberculous party and a readiness to make whatever sacrifice may be necessary in consequence of it. A person with active tuberculosis should not get married. An exception may be made when the conditions for recovery would be definitely improved by the change in the social state. A person with open ulcerative tuberculosis should be cautious about getting married. When it can be foreseen that nothing in the married state can interfere with physical well-being and happiness it is safe to get married. The prospective consort should be fully informed of the condition of the patient and of the danger to himself and any child which may be born. A person who has recovered from tuberculosis without having had open ulcers is free to get married without restriction of any kind. A tuberculous woman should be carefully watched and scientifically treated during the entire period of pregnancy and for at least six months after parturition. If the disease is at all active she should be kept at complete rest in bed. The diet must be nutritious. easily digested and easily assimilable. Her emunctories should be kept active. The weight of evidence is against the idea that the tubercle bacillus can be transmitted to the offspring through the milk. There is a definite benefit to the mother in nursing the child for at least six weeks after parturition, because this aids involution of the uterus. After six weeks the child may be weaned to save the drain upon the mother.—*Pregnancy in Tuberculosis, L. F. Flick, Hospital Progress, 1920, i, no. 7.*

Nontuberculous Lung Changes Following Pneumonia.—The great prevalence of pneumonia during recent years, more especially during the pandemic of influenza, and its prominent rôle in the disease of our soldiers, has caused a notable increase of the incidence of this disease among the people. In view of these facts, it should be borne in mind that during the next few years a great many chronic nontuberculous lung changes will be encountered. Their recognition is important because of their similarity to pulmonary tuberculosis, and their confusion with it.—*Nontuberculous Lung Changes Following Pneumonia, E. N. Packard, J. Am. M. Ass., December 4, 1920, lxxv,* 1537.

Prophylaxis in Tuberculosis.—Bacillary infection is compatible in the great majority of the human and bovine species with every appearance of health. Koch's bacillus usually remains a harmless parasite. Massive infections alone, occurring in children or adults free from any previous infection, result at once in a local or general disease of the lymphatic system. The most usual types of this disease are: (1) The acute miliary, nearly always rapidly fatal. (2) The bacillary septicemic, of which the gravity is in direct relation to the origin, virulence and number of the infecting microbes. (3) Benign infections which after remaining for many years occult or latent produce specific resistance to a new infection. When the latter is superimposed, it provokes Koch's phenomenon. The infected organism then tends to drive the bacilli to the surface, forming abscesses in which caseation takes place. The resulting forms of tuberculosis usually evolve slowly. They present a most serious danger through the diffusion of infectious material. This is favored by travel and commerce, the crowding of people into towns, bad ventilation and insufficient sunlight, and ignorance of evading contagion. These sowers of germs and the germs they sow are so numerous that 55 per cent of townbred children are already contaminated at the age of five years, and that after the fifteenth year scarcely 5 per cent of the total population remains completely free. The defensive reactions with which the organism opposes infection vary with different individuals. Age, integrity of lymphatic organs, the condition of the heart, vessels, lungs, liver, kidney, skin, the modality of nutrition and respiratory exchange play a rôle in every case. Everyone combats infection with natural arms: leucocytes, lymphatic glands, cellular ferments, hereditary or acquired powers of resistance or of intolerance towards the bacillus, The improvement of the material conditions of living, compulsory insurance laws, increased wages for the workers and the abolition of alcoholism will limit the possibility of contagion. But antituberculosis action can only be truly effective when individuals and communities are guarded against bacilliary infections and especially reinfections which give rise to grave and contagious forms of tuberculosis. Those who react positively to tuberculin, although they may appear perfectly healthy, intermittently eliminate and distribute virulent tubercle bacilli. Because of this intermittent feature they are very difficult to find. Every healthy individual who gives a positive reaction to tuberculin ought to be considered as suspect. Young children and young animals must be prevented from drinking unsafe milk which has not been heated at least 30 minutes at 70°C., or 15 minutes at 80°C. Contamination of food by bacilli from dejecta must be avoided. It results not only through unclean hands, soiled linen, contaminated vegetables and fruits, but also through the medium of flies and by soil or dust coming from fields which have been manured. Vaccination of all men and animals who are tuberculizable is the only means of limiting tuberculous infection and ultimately extinguishing it. It is a practical possibility since it is effected spontaneously in an immense number of individuals. Undoubtedly it would be dangerous to provoke such infections artificially by the use of virulent tubercle bacilli. But it is possible to modify certain properties of these bacilli in such a way that they become incapable of producing those cellular changes characteristic of tubercle.—*Prophylaxis in Tuberculosis, A. Calmette, Tubercle, November, 1920, ii, 49.*

The Bovine Bacillus and Man.—The diversity of views expressed in the correspondence on tuberculous milk shows that much work remains to be done, in comparative medicine and pathology, before a final decision can be reached as to the exact part played by milk in the spread of tuberculosis. Calmette states that the specificity of human or bovine bacilli is not absolute. Eber succeeded in infecting calves with human bacilli after passage through guinea pigs, and recovered from the lesions in the calf bacilli which appeared to have the bovine character, while cultures taken direct from the human sources employed in the experiment had the human characters. The possibility of transforming the one type into the other cannot be regarded as conclusively proved by these experiments, and it cannot be asserted that such a transformation habitually occurs in nature, but it would be dangerous to assume this transformation impossible. Bovine tuberculosis, where it exists, constitutes a real menace to man on account of the susceptibility of young children to this type of infection. The mode of entry of the bovine bacillus is mainly by ingestion of tuberculous milk. Since infants are clearly susceptible to bovine infection, they should be protected against the opportunities of contamination. It must be recognized that the principal source of human contagion is familiar, and measures of protection must be framed with this fact in mind. While it may be admitted that early slight infection may produce resistant individuals, such persons require guarding against later infections lest they increase the already large numbers of disseminators of tuberculosis.—*Tuberculosis, Leading Article, Brit. M. J., December 11, 1920, 906.*

Tuberculosis-Free Accredited Herds.—List No. 3 of herds officially accredited as free from tuberculosis, giving results to June 30, 1920, has been issued by the Bureau of Animal Industry. It shows that there have been established as fully accredited 3370 herds containing 82,986 cattle (48,471 purebred and 34,515 grade), and that 16,599 herds containing 257,577 cattle have been tested once without reactors. The number of accredited herds almost trebled within a year. Minnesota has the largest number, and next come Virginia, Wisconsin and Pennsylvania. In the work of tuberculosis eradication during the last fiscal year the Federal and State veterinarians applied the tuberculin test to 695,364 cattle, of which 28,616, or slightly more than 4 per cent, reacted.—*Communications, J. Am. Vet. M. Ass., December, 1920, lviii, 367.*

Eradication of Bovine Tuberculosis.—The work of tuberculosis eradication in the past has been impeded by a lack of coöperation between the Federal Department of Agriculture and the various state officials, by a lack of concerted action on the part of the veterinary profession, by a lack of sufficient funds provided to finance the work, by ignorance and prejudice on the part of many cattle owners, and by indifference to the menace of the disease on the part of the public in general. One by one these barriers are being broken down. Public sentiment is now strongly in favor of tuberculosis eradication. Coöperation between the State and Federal Departments of Agriculture is now being carried on successfully in 43 states. An average of about 60,000 cattle are being tested or retested monthly in the U. S. by government and state inspectors. At present the average number of reactors being uncovered monthly in the United States is about 4 per cent of the number tested. The number of reactors found shows a constant but slow decrease. Testing of range animals to a greater extent will be necessary before tuberculosis can be entirely eliminated. In the United States about 750,000 animals were tested for tuberculosis in 1919, which represents a small percentage of the 65,000,000 cattle population. During the past year there have been regularly employed in tuberculosis an average of about 250 veterinarians. The work requires at least 10 times this number. The salaries and personal expenses of these men, the indemnities paid for reactors and incidental expenses will bring the total amount to $20,000,000 annually. A law requiring the tuberculin testing of all cattle offered for sale at public auction should be incorporated upon the books of every state. There may be instances where the Bang system of placing tuberculous animals in quarantine has worked out to good advantage, but this system has been so abused in the past, and the advantages have been so remote that it should be discontinued. The intracutaneous test has done more in the past few years to promote tuberculin testing than any other factor. The speed with which the work can be carried on and the small inconvenience to the cattle owner as compared with the old subcutaneous method are its two most prominent features. Now that the United States Department of Agriculture has accepted this test, more work will be accomplished with the same force of inspectors.—*The Eradication of Bovine Tuberculosis, C. Ackley, Am. J. Vet. Med., October, 1920, xv, 473.*

Coöperative Eradication Campaign and the Practitioner.—Coöperative tuberculosis eradication is the embodiment of the greatest advance in bovine tuberculosis since the organism was first isolated and tuberculin was discovered as a diagnostic agent. Any veterinary practitioner who does not look upon this work in this light is either lacking in broadness of vision or is selfish enough to put personal gain in advance of a great public good. The eradication of tuberculosis requires systematized, concentrated tuberculin testing by men who can make a special study of it and devote their time to it. The author objects strongly, however, to Federal or State authorities interfering with legitimate practice by allowing their own men to test herds the owners of which are regular clients of other veterinarians in the same community.—*How the Coöperative Tuberculosis Eradication Campaign Affects and Appears to the Practitioner, J. F. DeVine, J. A. Vet. M. Ass., January, 1921, lviii, 458.*

Pioneer Work in Tuberculosis Control.—The first tuberculin test made on this continent was applied in 1892 near Villa Nova, 20 miles west of Philadelphia, to a herd of purebred Jersey cattle by L. Pearson. There were 79 cattle in the herd, some of them imported and all purebred; and 51 reacted to the test. On March 16, 1892, six of them were brought to the veterinary school and killed for postmortem examination. Pearson was a student in Germany in 1890 when Koch discovered tuberculin. During the following three years Pearson used the tuberculin test in his private practice. Its efficiency and reliability were recognized by veterinarians, physicians, sanitary officials and the more progressive livestock owners when they became more familiar with it. But the opposition of some of the livestock owners and journals continued for a long time. In 1895, when the Pennsylvania State Livestock Sanitary Board was organized and Pearson became its secretary, he introduced the principle of testing herds on the voluntary application of the owner. This principle was the keystone of what became known as the Pennsylvania plan for controlling tuberculosis, and it is also one of the features of the accredited herd plan. Viewed from a purely economic standpoint, and laying aside the question of public health, the control and eradication of tuberculosis in cattle is a matter of great importance not only to the cattle owner, but also to all consumers of meat and milk.—*Pioneer Work in Tuberculosis Control, L. A. Klein, J. Am. Vet. M. Ass., January, 1921, lviii, 455.*

Immunity to Tuberculosis.—In discussing in particular the immunity of the skin to tuberculosis, Edel relates the case of a woman with lupus who developed pulmonary tuberculosis after the lupus had been cured. The lung lesions also subsided under treatment, but then the lupus recurred. He ascribes this to production of antibodies in one local process which kept the other local process under control; when this was cured, the other got a chance to flare up.—*Immuniteit en tuberculose, K. Edel, Nederl. Tijdschr. f. Geneesk., October 16, 1920, lxiv, 1522.*

Control of Air Dustiness.—There are certain principal occupations that tend to produce characteristic fibroid changes in the lungs, designated as pneumokoniosis. This predisposes the worker to infection with tubercle bacilli. Typical trades are those followed by cutlery makers, filers, grinders, abrasive workers, polishers, buffers, manufacturers of jewelry, brass workers, finishers, sand blasters, saw filers, tool makers, glass workers, marble and stone quarry men, molders, potters, and miners of copper, gold, silver, graphite, iron, lead, zinc, mica, phosphate, spar, and quicksilver. Certain standard methods for air purification have been instituted in industrial plants. They take the form of hoods, exhausts, and fume lines usually beginning at or near the work plane and following certain engineering specifications, exhausting at a place sufficiently remote and protected to control the hazards arising from the occupation. In certain occupations where it has been thought that such fume lines could not be satisfactorily installed and operated, wet processes have been introduced. In point of origin, the wet process antedates the exhaust as a means of controlling dusty operations. To a large extent these two processes have given a sense of security to the operator and the operative. A survey of a plant was made by Scientific Assistant Myron Bantrell and dust samples, from which counts were made, were taken in various rooms of the plant. The counts were of one-fourth standard unit dust particles and ranged in number from 69,000 on the roof of the building to 4,548,000 in the grinding room. These conditions prevailed notwithstanding the fact that the management complied with the state laws in every way in its wet-grinding process, using a special compound of oil and water. This survey brings out the important fact that even a strict compliance with the present laws in regard to wet grinding does not always prevent a dust hazard, and that it is necessary to have some definite method of checking up the efficiency of dust prevention devices after their installation. The present methods used for removing dusts are subject to many faults and defects, and it is only by an actual dust count at the plane of work and in the room or at the place where the process is being conducted that we can determine the efficiency of the system and the amount of protection that is afforded the worker. Tentative standards of dustiness can be created by making dust counts in any place and under any conditions desired, pending a study of living conditions. The needs in the study of the control of air dustiness are: (1) The necessity for establishing a standard dust table of the number of dust particles of a certain size permissible in all dust-creating or dust-hazardous processes and occupations. (2) The necessity for checking the efficiency of all dust-removing systems or devices at regular intervals by an actual dust count at the plane of work and in the work room, which count must come within the limits prescribed by the standard dust table for that particular process. If in addition to these measures intensive education of employees as to their constant danger of tuberculous infection at home and in the plant is carried out and workers come to realize the hazards to which they are subjected, the present industrial mortality rate from tuberculosis may be expected to be lowered to that of the ordinary death rate.—*Recent Experiments in the Control of Air Dustiness, O. M. Spencer, Pub. Health Rep., December 3, 1920, xxxv, 2907.*

Control of the Factory Dust Problem.—There are two distinct factors involved in the production of an active case of tuberculosis—the number and virulence of the invading germs and vital resistance; but as to the relative significance of these two factors there is no general consensus of agreement. To the sanitarian who is actively engaged in the daily struggle against preventable disease it is a relief to turn to one phase of the tuberculosis problem where his feet rest on firm ground. In certain trades and occupations there is found a definite condition—the presence in the atmosphere of fine particles of mineral and metallic dust—so clearly associated with an enormous excess of respiratory mortality as to leave no reasonable doubt that the dust is the effective factor in causing the disease. The object of this paper is to review the evidence which indicates a direct causal connection between atmospheric dust and industrial tuberculosis, and to point out the practical methods by which the hazards of the dusty trades may be practically controlled. Data obtained in regard to the prevalence of occupational disease in different countries and at different periods of time must be interpreted with great caution on account of the fact that industrial processes differ so widely and change so frequently. Data should be available in the form of actual death rates, based on knowledge of the population exposed as well as on the number of deaths occurring and properly corrected for the age distribution of the group involved. Three important statistical studies have been made in the United States during the past decade. The first of these is contained in bulletins of the U. S. Bureau of the Census giving the proportionate mortality by occupations of the population of the registration area for 1908 and 1909. The second is a bulletin on the industrial experience of the Metropolitan Life Insurance Company, by L. I. Dublin. The third is contained in a series of monographs by F. L. Hoffman of the Prudential Insurance Company. It seems evident that a comparison between the Prudential figures for a given dusty trade and the census figures for all occupied males is not a fair one. Besides, the conclusion is unwarranted that the iron and steel workers experience an excessively high death rate from tuberculosis as the result of the dust hazard. Even when comparisons are made in the correct manner between a dusty trade and an average group of as nearly as possible the same general social and economic status, there must always be a large measure of doubt in regard to the significance of high tuberculosis ratios. Ratios as distinct from dates, depend on two independent variables, and a high ratio of tuberculosis deaths may be produced by a low mortality from other causes, as well as by a high mortality from tuberculosis. In England numerous statistics are available which indicate that in many industrial employments, such as metal mining, marble and stone cutting, and grinding and polishing, high tuberculosis ratios are associated with high tuberculosis rates. Even in a trade like pottery making, which is generally considered as one of the industries most affected with plumbism, the latter is far less important as a factor in the death rate than is industrial tuberculosis. In the United States the only general collection of statistics was presented in a special bulletin prepared by the Bureau of the Census for the meeting of the International Congress of Tuberculosis. The absence of an analysis by age periods detracts seriously from the value of the results. The high rates among cigar makers and tobacco workers, compositors, printers and pressmen, servants, bookkeepers, clerks and copyists, and the low rates among bankers, brokers and officials of companies are no doubt due to the age composition of the respective groups. The entire population of the mill district shows a tuberculosis rate of 200 as compared with 150 for the state as a whole. The mill population itself has a rate rising to 650, and the group of polishers and grinders a rate of 1900. The other employees of the mill are not entirely comparable in age, race, and general social and economic status with the polishers and grinders, but it is evident that the high death rate among the latter is primarily due to the hazards of their occupation. In every instance in which a heavy incidence of tuberculosis has been clearly shown to result from exposure to industrial dust, the dust in question has been in part, at least, made up of crystalline rock. Silicosis produces miners' phthisis and is probably the chief factor in the tuberculosis among axe grinders. Exposure to lime and cement dust appears not to be associated with high tuberculosis rates. Coal dust, if it has any effect, appears to exert a protective influence against the invasion of the tubercle bacillus. A clearly marked fibrosis, anthracosis, follows the inhalation of coal dust, and this condition appears to favor a high mortality from acute respiratory disease; but the tuberculosis death rate among coal miners is uniformly and characteristically low. The reason for this difference between the effects of different dusts is still largely a matter of speculation. It may be due to physical or chemical influences. With regard to a great intermediate group of other industries which have commonly been classed as dusty trades, the authors are inclined to await further and better statistical evidence before reaching a final conclusion as to the existence of industrial tuberculosis. —*Industrial Tuberculosis and the Control of the Factory Dust Problem, C.-E. A. Winslow and L. Greenburg, J. Indust. Hyg., January, 1921, ii, 333.*

Racial Differences in Tuberculosis.—From a table showing the incidence and mortality of tuberculosis in the British Expeditionary Force in France in 1918 it is evident that the incidence and mortality vary inversely with the degree of possibility of previous contact with the tubercle bacillus. The Africans, both the Kaffirs of the South African Native Labor Corps and the Cape Boys of the Cape Colored Labor Corps show an appalling incidence and mortality. The Indian Native Labor Corps comes next, then the Chinese. The incidence and mortality of the British troops, drawn from the almost universally infected communities of a highly organized and largely urban population, are relatively inconsiderable. Here there can be no question of alcoholic excesses, bad housing, insanitary surroundings or unsuitable food. The suggestion that there is an hereditary tendency more marked among the children of tuberculous parents than in the rest of the community must be seriously called in question in view of the extreme susceptibility shown by persons coming from a parent stock in which no tuberculous taint can have existed. The essential factor in susceptibility would appear to be largely unconnected with race, but to depend rather upon an absence of acquired resistance to infection. This acquired resistance can only be attained by contact with the tubercle bacillus. It is probable that the diminution in the tuberculosis death rate so marked throughout Great Britain in the last fifty years has depended less upon the efforts of stamping out tuberculosis than upon the natural processes of autoimmunization that have gone on coincidently with the developments of industrial life. While there should be no slackening of the effort to control the spread of infection, it should be clearly recognized that this infection is much more dangerous at certain periods of life and to certain individuals than to the community in general. Infants and young children are virgin soil. If the efforts of all those engaged in attempting to prevent the spread of tubercle bacilli, human and bovine, were so far successful as to ensure that every young man and woman reached the wage-earning period without any contact with the germ, it is possible that the whole population would end by being as susceptible to infection as are the African tribesmen in their native isolation. This equivocal success is never likely to be obtained, and we are quite safe in doing all we can to guard against infection. Our best efforts can hardly do more than ensure that the omnipresent tubercle bacilli shall be ingested in minimal immunizing doses, rather than in such quantities as to prove too much for the gradually developing resistance. The future of tuberculosis prevention lies in the deliberate exploitation of immunization by means of vaccinating doses of dead or attenuated bacilli.—*Racial Differences in Susceptibility to Tuberculosis, S. L. Cummins, Brit. J. Tuberc., October 1920, xiv, 160.*

Tuberculosis in Soldiers.—Valuable lessons can be learned from experiences in the army and among prisoners of war in regard to prevention and treatment of tuberculosis. Chief among them is the necessity for not limiting the search for tuberculosis to those with active lesions or the suspects. Those predisposed to the disease can be recognized by their physical aspect, the vertical, pendulum or drop heart, movable ninth and tenth rib, asthenia, dyspepsia, low pressure, tachycardia, the morbid susceptibility of the respiratory apparatus, "respiratory claudication" and respiratory incapacity of the apex, but above all by the diminution of vital capacity, hypotrophy and tenderness of the outer margin of the trapezius, and hypertrophy of the sternocleidomastoid, especially on the sound side. The amyotrophy and tenderness of the trapezius are not consequences but accompaniments of the tuberculous process, as also the sinking in of the chest wall and the diminished expansion. They may even precede manifest lesions as they are a neurotrophic reflex between the lung and the respiratory muscles. In radioscopy, special attention should be paid to the smaller size of the lung space above the clavicle, especially if unilateral, to its less distinct aspect, and to the lesser movability of the diaphragm. Differentiation is rendered easier by the fact that in other pathologic conditions the lesions are liable to change about and vary from time to time, while the tuberculous are comparatively stable.—*Rilievi sulla tubercolosi polmonare nei soldati e nei prigionieri di guerra, G. Boeri, Rif. Med., August 14, 1920, xxxvi, 736.*

The Mononuclear Phagocytes of the Lung.—In the present state of our knowledge, there is no reason to believe that free independent cells, endowed with the faculties of amoeboid movement and phagocytic activity arise from the tissues broadly classed under the term epithelium. It is clear that the mononuclear phagocytes of the lung are cells possessing these qualities. The present study was undertaken with the object of obtaining further data on this subject. It is limited to the reactions as found in the lungs of experimental animals, following the intratracheal injection of foreign particulate matter. Vital staining was also used to mark the large mononuclear wandering cells, after the method of Sewell. Rabbits and guinea pigs were employed, but rabbits were more suitable for repeated intravenous injections. The stain was injected intravenously in doses of about 5 cc. daily, except Sunday. The findings in the lung in vitally stained but otherwise normal animals would indicate that there is a succession of endothelial cells proliferated from the capillary linings which wander into the alveoli. These cells take up vital stains fairly readily during proliferation and are thus more or less definitely marked and may be identified in their subsequent activities. These cells are demonstrated in the experimental animal not only as morphologically identical with the dust phagocytes of the alveoli, but also to serve as dust phagocytes in the alveoli. The pigment has been shown to be rapidly taken up by large mononuclear phagocytes, which show the morphological characters and faculty of amoeboid movement possessed by the wandering mononuclear endothelial cells. The origin of these cells has been shown to be by proliferation from the endothelial cells lining the blood capillaries of the alveolar walls, whence the newly formed cells migrate directly into the alveolar spaces by passing between the cells lining the alveolus, to take up their phagocytic function. From their field of activity in the air sacs, these phagocytes have been found slowly returning to the interstitial tissues of the lung with their loads of carmine, and carbon particles frequently, wandering very gradually into the terminal lymphatics and so along these channels to their eventual goal, the peribronchial lymph node. Anthracosis in the animals used only served to emphasize the similarity of the response in the experimental procedure to that in the natural process of anthracosis. The author's findings are in agreement with the recent studies of Foot. The whole mechanism of dealing with foreign particles of essentially inert materials in the lung, as found in the natural event of anthracosis, or in the broadly similar lesions artificially induced in various ways seems inadequate and rather of the nature of a makeshift. Such materials, gaining entrance to lung alveoli, seemingly constitute a type of irritant for which there has not been developed a perfect defense mechanism, so that the process known as anthracosis is the result of failure on the part of the moist membranes of the upper respiratory tract and the ciliated epithelium of the bronchial tree to remove foreign particles from the body. This failure makes every city dweller subject to a slight but constant accumulation of an irritant unavoidably inspired into the ultimate alveoli, where it sets up a reaction similar to that against a mildly irritating foreign body in any tissue. The end results of this process have been discussed by Klotz and Haythorn. What has been said of the disposal of foreign inert materials also holds true for tubercle bacilli. It is believed by Permar that by analogy a clear picture of the mode of origin of the isolated tuberculous lesions in the peribronchial lymph nodes can be formed.—*An Experimental Study of the Mononuclear Phagocytes of the Lung, H. H. Permar, J. Med. Research, July-September, 1920, xlii, 9.*

Tubercle Bacillus as Fat Fungus (Fettpilz).—The extensive investigations of the conditions for the fatty degeneration of fungus cells which have been carried on during the last five years in the *Institut für Gärungsgewerbe* by Lindner and his coworkers with the support of the war committee for oils and fats have shown that the tubercle bacillus like the Eudomyces vernalis can undergo such fatty degeneration as to lose its reproductive powers. Sugar and alcohol and alcoholic vapors inhibit the growth of Eudomyces vernalis by causing fatty degeneration. This degeneration is impossible without sufficient oxygen. The dried tubercle bacilli contain 42 per cent fat. This is the cause of their acidfast properties. Alcohol has a noxious result on the tubercle bacilli in vivo. In some sanatoria large doses of alcohol are given empirically. To produce fatty degeneration alcohol and oxygen must act together on the tubercle bacilli. The rest cure in the open increases the oxygen content of the blood; good food with measured doses of alcohol or sugar furnish the other prerequisites for the fatty degeneration of the tubercle bacilli. With the present high cost of alcohol the inhalation of weak alcohol vapors may be more expedient. Thus the fat fungus biology opens a new perspective for the fight against tuberculosis by means of old approved remedies.—*Neue Wege zur Bekämpfung des Tuberkelbazillus in seiner Eigenschaft als Fettpilz, P. Lindner, Tuberculosis, October, 1920, 250.*

Effect of Amino Acids on the Growth of Tubercle Bacilli.—Tubercle bacilli were grown in two sets of broth. Both had a glycerol-meat infusion basis, but A contained 2 per cent Difco peptone and B 1.7 per cent Difco peptone plus 0.3 per cent aminoids. A analyzed as follows: solids 9.22 per cent, ash 1.05 per cent, phosphoric acid 0.116 per cent, nitrogen 0.348 per cent, nitrogen precipitated by zinc sulphate 0.110 per cent, and nitrogen as amino acids 0.098 per cent. The corresponding figures for B were 9.19 per cent, 1.00 per cent, 1.76 per cent, 0.369 per cent, 0.098 per cent, and 0.13 per cent showing a marked increase in phosphoric acid and amino acid nitrogen. Growth of the tubercle bacillus was much better on B. Varying concentrations of aminoids were tried and 0.3 to 0.5 per cent found most satisfactory. Increased growth was probably due to the increased phosphorus as well as amino acid nitrogen, phosphorus being an important constituent of the tubercle bacillus in lecithin and nuclei acid molecules. The osmotic pressures of plain and glycerol broth (5 per cent glycerol) were compared and found to be 7.2 to 10.8 atmospheres and 31 atmospheres, the glycerol thus increasing osmotic pressure threefold.—*A Note on the Effect of Amino Acids on the Growth of Tubercle Bacilli, P. Masucci, J. Lab. & Clin. Med., November, 1920, vi, 96.*

Morphology of the Sputum in Pulmonary Tuberculosis.—In a previous communication a method had been described for the morphological study of the cells in sputum. The principle of this method was the wet fixation of the smear. The sputum is collected in a sterile Petri dish and examined at once. A smear is made with light pressure. This is fixed in absolute methyl or ethyl alcohol for three to five minutes, or the slide may be fixed in the stain for three minutes. The stain is 1 per cent methyl alcoholic solution of magdala red, 1 part, 1 per cent methyl alcoholic solution of thionin or toluidin blue, 20 parts—mixed just before use, diluted with equal parts of distilled water and allowed to stand for thirty minutes. Wash, blot and before drying add or place in absolute alcohol for three minutes. Add xylol until the smear is transparent, blot, add cedar oil and cover with glass. By this method nuclei are stained with the thionin or toluidin blue, also all basophile subtances. Magdala red stains the acidophile substances, namely, eosinophile granules, Charcot-Leyden crystals, etc.

The results are embodied in the following conclusions: (1) Phagocytosis of tubercle bacilli is a frequent occurrence in the sputum. It is of no prognostic significance. In 92 instances it was absent in only three. Polymorphonuclear neutrophiles, and exceptionally alveolar epithelium, are phagocytic. As many as 40 bacilli were counted in a microphage or small phagocyte. Phagocytosis varies in the same patient within short periods. (2) Size and morphologic characteristics of the bacilli are of no prognostic significance. The occurrence of short rods in acutely progressing cases is confirmed. Branched, thread-like or clubbed forms are frequently found. Possibly these are degeneration forms. (3) Eosinophiles are frequently found in the sputum of the tuberculous. Mast cells are seldom seen. There is no connection between the presence of eosinophiles and asthma. They have no prognostic significance. (4) Epithelioid cells are frequently found in the sputum. They occur singly or bound together, and may lead to the formation of giant cells. Confusion with lymphocytes is possible. (5) Giant cells from macrophages of the sputum are described. Typical Langhans cells were occasionally seen in unfavorably progressing cases.—*Untersuchungen über die Morphologie des Auswurfes bei Lungentuberkulose, E. Liebman, Zeitschr. f. Tuberk., September, 1920, xxxii, 341.*

Bacterial Flora of Tuberculous Sputum.—Strobel carried on these investigations while on temporary relief duty at the Meriden Tuberculosis Sanatorium, Meriden, Conn. The following problem presented itself: Is there any morphological change in the tubercle bacillus before, during or after hemoptysis, and is there a constant presence of Gram positive cocci? Only 5 hemorrhages occurred during Strobel's presence at the sanatorium. In all, acidfast bacilli were found, presenting a markedly granular or broken-down rod which held the stain well against an acid. Gram positive cocci were observed in all specimens. These were arranged singly, in pairs, in chains and in tetrads. From these specimens guinea pigs were inoculated without any previous chemical treatment of the sputum. One pig died twenty-two hours after injection. The liver and spleen were greatly enlarged and adherent to the stomach. Large tubercle bacilli were found in abundance in smears from all organs. The second pig died thirty-five days after inoculation. Lymph nodes, liver and spleen were greatly enlarged and the intestines were matted together by numerous adhesions. On the right they were strongly adherent to the parietes; on the left there was a large abscess. Smears from all these organs contained abundant tubercle bacilli. No Gram positive organisms were found in smears from these autopsies. Later 4 more hemorrhages occurred. The sputum of all contained tubercle bacilli and Gram positive cocci. A rabbit was inoculated with sputum from each of these cases. One rabbit died in twenty-four hours showing marked congestion of the lungs and liver. Blood smears contained large encapsulated diplococci in great numbers. The second rabbit died on the ninth day. There was a severe peritonitis. Encapsulated diplococci, but no tubercle bacilli, were found in the pus. The other two rabbits died of lobar pneumonia and pneumococcic septicemia. In all patients after hemorrhage had ceased the microscopic picture of the sputum had not changed. There were therefore two widely different infections in these animals. The guinea pigs died from an extremely virulent tubercle infection, while the rabbits undoubtedly died from the effects of the pneumococcus. It is concluded that no relation existed between the Gram positive cocci and the acidfast bacilli in these instances. The marked beading of the tubercle bacilli originally was probably due to the poor culture medium in which it was growing. As soon as the culture medium was improved (guinea pig) they began to grow luxuriantly. —*The Bacterial Flora of Tuberculous Sputum, J. E. Strobel, Med. Rec., December 25, 1920, xcviii, 1060.*

Value of Inspection in Diagnosis of Tuberculosis.—The importance of inspection in the diagnosis of pulmonary tuberculosis is emphasized inasmuch as the findings so obtained often will lead to a diagnosis. However, other aids should not be neglected. Tuberculosis, although the lesion may be localized, manifests itself by secondary changes in every organ of the body; in fact, in every tissue, and these changes may be perceived by inspection. For example, two types of hands are found, the one where the ends of the fingers are clubbed, the other where they are long and thin and tapering. The curvature of the nails is accentuated, not only laterally but longitudinally. The color of the nails is interesting and important. Attention should be directed to the arms, the axillae, the head and the neck; the hair, the facies, the ears, the eyes, the color of the cheeks, the chin and the jaw, the mouth, the tongue and the chest. Much information may be obtained in this way and serve as a basis for a diagnosis, when accessory aids to diagnosis have failed.—*Practical Points in Diagnosis of Pulmonary Tuberculosis, J. Crockett, Glasgow M. J., September, 1920, cxiv, 129.*

Differential Diagnosis of Early Tuberculous Joints.—In a short note emphasis is laid upon the fact that obscure joint disease which responds favorably both in subjective symptoms and objective signs to hot air treatment is usually nontuberculous in origin. Tuberculous joints, on the other hand, show no improvement when so treated. —*Zur Differentialdiagnose bei beginnenden tuberkulösen Gelenkerkrankungen, J. Oehler, Münch. med. Wchnschr., July 16, 1920, lxvii, 845.*

Diagnosis of Active Pulmonary Tuberculosis.—From an analysis of 67 cases in which 150 differential counts of the white cells, together with Arneth counts, were made, and of 30 cases in which 250 total counts were estimated, the following conclusions were reached: (1) If consecutive daily leucocyte counts are made a variation of total numbers of white cells is found in all active cases of pulmonary tuberculosis—a variation in excess of that occurring normally in health. (2) Physical signs in the chest may give little or no help in determining the activity of a lesion. For instance, a cavity in the lung may be followed by pathologic repair and clinical quiescence, and in such a case the total leucocyte count may be small, and the Arneth count but slightly altered. Conversely, there may be a definite "leucocyte swing" and a marked "deviation to the left," in cases showing no other objective sign of active disease. (3) The total leucocyte count bears a definite relationship to the acuteness of the lesion in the chest, and the acuteness of the lesion has, in turn, a more or less intimate connection with the presence of organisms other than the tubercle bacillus. (4) The Arneth deviation to the left (a phrase synonymous with an increase in cells of class I and II, that is, those with one or two nuclear segments) is established in all cases of active disease. The more severe the infection the greater is the deviation to the left. (5) An approximation of the quantitative and qualitative blood picture to the normal is a favorable sign and indicates quiescence.—*A Contribution to the Diagnosis of Active Pulmonary Tuberculosis, J. B. McDougall, Lancet, August 21, 1920, cxcix, 390.*

Complement Fixation. — Tests were made on patients with gastrointestinal disturbances regardless of the presence or absence of clinical tuberculosis. Contrary to the opinion of Ives and Singer, two cases of arrested tuberculosis gave positive reactions. On the other hand clinically active cases gave negative reactions. The principle of Hecht was therefore tried. In the original complement fixation technic, the amboceptor is not destroyed, and in addition a titrated amount of amboceptor is added. An excess of amboceptor is thus present in the serum, consequently giving a negative reaction when it really should be positive. The Hecht modification tries to avoid this error, Petroff, Miller and Fleischer-Ives antigens were used. In the Hecht modification, the hemolytic index of the blood examined was determined by adding varying amounts of normal saline to 0.1 cc. unheated serum. With the original method there were 4.98 per cent positive reactions, in cases diagnosed non-tuberculous. The Hecht modification gave 9.96 per cent. Of 10 tuberculosis suspects, the original technic gave one, the modification two strongly positive fixation tests. Of eleven cases of clinical tuberculosis, four or 39.6 per cent were positive with the original technic, six or 59.4 per cent with the modification. The modification, therefore, gives a larger percentage of positive results than the original technic. The Petroff antigen gave more positive results with the original and modified technics than did the Miller or Fleischer-Ives antigens.—*The Value of Complement Fixation Test in Tuberculosis, Roy Upham and A. J. Blaivas, J. Lab. & Clin. Med., September, 1920, v, 784.*

Differential Diagnosis of Tuberculosis.—A correct positive diagnosis is much oftener missed than it is wrongly made. Most nontuberculous diseases of the lungs occur in the middle or lower lobes. When the apex is clear only positive sputum should justify a diagnosis of tuberculosis. Most nontuberculous diseases of the lungs are comparable only with advanced tuberculous disease. When tubercle bacilli are absent after repeated examinations, the disease must be referred to some other cause than tuberculosis, even if the symptoms and physical signs are those of an advanced tuberculosis. A patient should not be condemned as tuberculous upon a suspicion. Spitting of blood may come from many causes, and alone does not justify a diagnosis of active tuberculosis. The differential diagnosis is sometimes difficult or impossible at the first examination, and requires time and observation. Diseases of the upper respiratory tract, like chronic pharyngitis, adenoids, diseased tonsils or nasal sinuses, may produce a chronic cough, blood-streaked sputum, rise of temperature, loss of weight and strength, but tachycardia and bacilli in the sputum are absent. The cough is likely to be more pronounced and may have lasted for years. Bronchopneumonia and lobar pneumonia may be the beginning of an acute tuberculosis. Time alone can differentiate. In subacute or avirulent lobar pneumonia the physical signs may persist for a considerable time together with the cough and sputum. The physical signs, however, are at the base and the sputum is negative. In influenza, the sputum is purulent and constantly free from tubercle bacilli, and the constitutional symptoms are not as marked or progressive as in tuberculosis. In bronchitis there is no impairment of resonance and the râles are generally confined to the base. The general condition of the patient is good. The association of asthma and tuberculosis is rare. Bronchiectasis may involve a large part of the lung; there may be one or more discoverable cavities. The physical signs are those of an advanced tuberculosis, and there is often hemoptysis, but tubercle bacilli are absent. Pulse and temperature are usually normal and there is no great deterioration of the general health. In empyema, abscess and gangrene of the lung the physical signs are in the middle and lower lobe. Exploratory puncture and the finding of leucocytosis together with absence of tubercle bacilli clear up the diagnosis. Cardiac lesions with hemoptysis, cough, emaciation, dyspnea on exertion and râles which may be in the apex are differentiated by the evidence of cardiac disease and the history. Other diseases to be differentiated from pulmonary tuberculosis are diseases of the pleura, cancer and syphilis of the lung, actinomycosis, aortic aneurysm, anemia, neurasthenia, dyspepsia, anorexia, and hyperthyroidism.—*The Differential Diagnosis of Tuberculosis, E. O. Otis, Boston M. & S. J., December 16, 1920, clxxxiii, 695.*

X-ray Examination of the Chest.—X-ray examination of the thorax has now reached a point where it should be regarded as a routine part of the examination and should no more be omitted than should auscultation or percussion. In any particular case it may yield no more information than has already been obtained by a clinical examination, but many times it will give the most unexpected results and radically alter diagnosis, prognosis and treatment. The radiologist and the clinician must coöperate. In fluoroscoping the chest the importance of diminished diaphragmatic movements has been recognized for years, but in Berry's experience there is a stage of diagnostic significance preceding that of actual limitation. This may take the form either of the diaphragm descending in a series of short, jerky movements instead of an even sweep, or it may be seen that the diaphragm on the affected side commences to descend later than on the normal side, though it eventually has the same range of movement. In studying structural changes, gross or fine alterations may be looked for. Gross changes can be seen on the screen; for the fine points plates must be used. Dilatation or aneurysm of the aorta can be recognized even though utterly unsuspected and may throw much light on the true diagnosis. Enlarged glands at the root are common and appear as shadows of varying density with somewhat hazy edges. If the glands are calcified the shadows are denser and the edges more clearly cut, this point referring also to nodules in the lung tissue. Areas of lung consolidation are denoted by shadows of various depths. Frequently a shadow which appears on the screen to be of homogeneous density is seen on the plate to consist of an aggregation of many smaller shadows overlapping each other to a greater or less extent. It should be noted whether the shadows show a lobar distribution, whether they are more marked in the mesial or peripheral portions of the lung, whether they follow the line of the bronchi, whether they are associated with glandular enlargement, whether there is any evidence of calcification. Cavities in a typical case are seen as more transparent areas which may be surrounded by a dense band representing sclerosed lung. Sometimes this sclerosed area is absent and the cavity may escape attention, as may also be the case if it be full of secretion at the time of examination. Occasionally a cavity is seen to be half full of fluid when the patient is erect, the upper limit occupying a horizontal line. In the root area especially, dilated bronchi with thickened walls may be mistaken for cavities. Thickening of the pleura is recognized by a uniform veiled appearance, either confined to a localized area or spread as a uniform fog over the entire side from base to apex. In pleural effusion the opacity is greater and the heart is usually displaced to the opposite side. Examination in the erect posture shows the upper border of the shadow as a curved line with the concavity upwards, the inner end of the lung being close to the lung root and the outer end on the axillary wall of the thorax on a higher level. If the fluid is free it spreads itself out when the patient is recumbent and casts a shadow of uniform density over the whole of one side of the thorax and may exactly simulate pleural thickening. Localized effusions enclosed by adhesions show considerable opacity with fairly defined edges. The typical empyema occurs on the lateral wall of the thorax, but localized effusions are also recognized on the diaphragm, the mediastinum and in the interlobar furrows. Pneumothorax and collapse of the lung are shown by unusually translucent areas in which no lung markings are visible. If the pleura be free from adhesions and the collapse complete the lung contracts to a small area around the root and will be shown as a dense shadow while the remainder of the hemithorax is unduly bright. Sometimes a small localized pneumothorax may simulate a cavity, especially when near the apex. If fluid be present in addition to air the appearance is very striking, the affected side showing a dense shadow in the lower part of the thorax and a very light area above, the dividing line being quite sharp and always horizontal, whatever the position of the patient. Waves may be seen on the surface of the fluid if the patient is shaken. Lung abscesses show as rather poorly defined areas of opacity with evidence of breaking down in the centre. Usually the root glands are enlarged and the appearance may be mistaken for lobar tuberculosis, but the small nodular shadows are missing. Lobar pneumonia gives a shadow corresponding to the area of the affected lobe, its density ranging from slight obscurity in the congestive stage to great opacity in the stage of hepatization. The picture of bronchopneumonia is very similar to that of disseminated tuberculosis. Chronic bronchitis leads to peribronchial thickening which must be distinguished from that of tuberculosis. Anthracosis and silicosis almost exactly simulate the appearance of disseminated tubercle except for the absence of nodules. In every case, the history and clinical course must be taken into consideration—*Basic Principles in X-ray Examination of the Chest, M. Berry, J. State Med., December, 1920, xxviii, 368.*

X-ray Diagnosis in Phthisis.—The large central shadow observed in the normal thorax is due to the heart and mediastinal contents. Extending out laterally are the heavy shadows caused by the large or stem bronchi. On the right side ascending and descending bronchi are distinctly seen, but on the left, due to the intervention of the cardiac shadow, the greater part of the descending bronchus is not visible. The density of these shadows increases with age, being as a rule much heavier in the adult. Radiating from these markings are finer lines which project into the lung field for varying distances, but do not extend normally to the surface of the lung. These markings are produced by the walls of the bronchi and the blood and lymph vessels with their contents. In the examination of an individual it must be determined what is normal for that individual. The identical roentgenogram may be perfectly normal for a man of seventy, but highly pathological in a man of twenty. Cases of chronic tuberculosis group themselves into those showing glandular involvement as in children, those showing peribronchial infiltration and those showing parenchymatous changes. Any or all of these types may be found in incipient or moderately advanced cases. In the glandular type of tuberculosis, whether seen in children or adults, there is a mediastinal group and a pulmonary group of glands to be considered. The mediastinal group includes all the tracheobronchial glands. These glands are located in the median line between the sternum and vertebral column. Unless enlarged to such an extent that they extend beyond the median shadow they are best seen in oblique position at the level of and above the sixth rib, posteriorly. Infection of these glands alone usually follows the infectious diseases of childhood and on examination is revealed as an indefinite shadow mass in the otherwise clear mediastinal space. The hilum group is made up of many intrapulmonary peribronchial glands. Involvement of this group often does not give rise to any special clinical symptoms and is found with simple bronchitis and bronchiectasis. It is well seen in dorsal or ventral plates, appearing as discrete areas of increased density more or less well defined, depending on the stage of the pathological change. An etiologic diagnosis cannot be made from the appearance of the roentgen plate or screen alone. There are, however, certain changes noted in the parenchyma and seen as minute islets of increased density in selected localities (the first and second interspaces near the median triangle and toward the periphery of the lung near the angle of the scapula) which represent conglomerate tubercles such as one sees on gross section of the lung at necropsy. The roentgen ray in the majority of cases reveals a more extensive lesion than is found by physical signs.

Not only the extent but the X-ray appearance of the lesions is of value in prognosis. The so called interlobar pneumothoraces which show as annular areas of increased density on the X-ray plate are often definite evidence of softening of the lung. These areas probably represent the so called silent cavity. They are seldom diagnosed clinically and indicate a somewhat graver prognosis. In experienced hands the question of activity can be decided by X-ray alone. Well defined calcified areas of increased density are old processes. Fibroid changes denote chronicity. Well walled-off cavities indicate healing. A cavity partially filled with pus, as well as hydro- and pyopneumothorax, denotes activity. Mediastinal shadows though dense often give no physical signs. Glands enlarged sufficiently to cast definite shadows are still beyond the reach of percussion and auscultation. Patients who on physical and constitutional signs are incipient pass on to a more advanced stage when examined by the X-ray and in some supposedly moderately advanced cases cavities are found where physical signs gave no evidence of them.—*X-ray Diagnosis in Phthisis, F. W. O'Brien, Boston M. & S. J., December 16, 1920, clxxxiii, 702.*

The Dunham Fan in Roentgenograms.—The Dunham fan is a triangular shaped increase of density on a roentgenogram usually found at the end of a trunk composed of a bronchiole, blood vessels, lymphatics and connective tissue. The size of the fan is determined by the number of lobules involved. The type of pathology influences the character of the density. In advanced conditions, there is a diffuse density with fans showing here and there, many of them irregular in size and shape. The characteristic marking of a plate of pulmonary tuberculosis consists of fan-shaped density with the apex toward the hilum, and the base toward the pleura, the apex being connected with the hilum by a heavy trunk. Two or more such areas indicate tuberculosis, the greatest density indicating the oldest lesion. There may be great variation of density in the fan, varying from radiating lines (known as linear markings) to a heavy blotting-out effect. The most striking characteristic lies in the varying degree of change in the different trunk groups, for one trunk may be involved while the one next to it may be absolutely clear. In the early adult cases the lesions are usually limited to the trunks of the upper lobes, particularly the first interspace trunk. If the linear markings are cottony or faintly obscured as by a cloud effect, and if the fan appears to be wide open, active tuberculosis must be considered. If the linear markings are sharply defined, dense, and show sharp studding beyond the trunk, with the fan partially closed, a healed lesion is to be suspected. Caseous bronchopneumonia gives a picture showing a definite, heavy flocculent density, usually in the more dependent parts of the lungs, rarely in the apices. The fan may or may not be seen. If the lesion is small and near the pleura, it is usually walled off by a heavy septum with flocculent densities beyond the trunk. If the lesion is large it is frequently impossible to make out the borders of the triangles. With a condition such as this there is usually an old lesion at the apex, and frequently a cavity is seen. In miliary tuberculosis the lung areas are spotted with fine, cottony granules of increased density, which may be discrete or confluent. They vary from faint shadow effects to brilliant discrete areas due to calcification. The calcified areas are distinguished from those of anthracosis by the fact that the latter are usually more stellate, sharper, and thicker. Before the Dunham fan was used in the roentgenological diagnosis of pulmonary tuberculosis, many early cases were overlooked.—*The Dunham Fan on Roentgenograms, P. S. Seabold, Philippine J. Sci., July, 1920, xvii, 105.*

Certain Symptomatological Aspects of Pulmonary Cavities in Tuberculosis.—Among the anatomicoclinical phases of pulmonary tuberculosis, the cavitary phase is the one that best retains its clinical individuality. In some patients who have reached the cavitary stage the general health remains good, and many do not present any of the classical signs of cavity on auscultation, the pulmonary lesion being detected by radiography. In the first place, there are silent cavities giving rise to no clinical signs, in which auscultation is almost normal so far as they are concerned. At the most does one find some incomplete percussion dulness and respiratory changes in these subjects. But there are cases of pulmonary cavitation with most deceptive symptoms and to these we would particularly call attention. There are cavities giving rise to evidences of dryness in which auscultation reveals only some crackling, an increase of the vibrations, and respiratory roughness. There are cavities giving rise to moist signs, with subcrepitant râles, moist, crackling sounds, and a blowing expiration. In these circumstances there are certainly no characteristic signs of a pulmonary cavity. The subcrepitant râles and dry crackling do not figure in the classical picture of pulmonary cavities, and in reality they usually merely indicate the condition of the pulmonary parenchyma lying between the cavity and the examiner's ear. From these facts some interesting conclusions can be drawn. The first is that the roentgen rays alone are able to reveal with certainty all pulmonary cavities, and Masselot of Tunis has shown that the frequency of unsuspected pulmonary cavities should lead to better prognoses in many cases. Once again is confirmed the general principle that the functional condition rules over the physical condition, and that in pulmonary tuberculosis in particular, the degree of tuberculous impregnation and the state or organic resistance of the subject are prognostic factors of far greater importance than the physical state of the patient. A tuberculous patient is not always to be condemned to death simply because he presents pulmonary cavities, but the condition is much more grave when the subject is hectic, no matter what may be the anatomical degree of the lesions present.—*Editorial Note, Med. Rec., December 11, 1920, xcviii, 989.*

Tenderness in Muscles as Early Sign of Tuberculous Lesion Beneath.—Reëxamination of soldiers who had been suspected of tuberculosis months before has demonstrated that those among the suspects, whose muscles in front of and behind the apex were tender, had all developed unmistakable tuberculous lesions in the interim. On the other hand, in those with normal muscles their suspicious cough and bronchitis had harmlessly subsided and they were apparently healthy. The man is examined in a room alone with two physicians; one at the back palpates the muscles while the other, in front, watches the subject's expression for a grimace of pain or for the dilatation of the pupil which occurs when sharp pain is felt.—*La recherche des troubles hyperesthésiques au niveau du relèvement musculaire des sommets peut-être utilisée pour le diagnostic précoce de certaines formes de tuberculose au cours des expertises médico-militaires, Molle, Lyon Med., October 10, 1920, xix,* 838.

The Determination of Activity According to Wildbolz.—Wildbolz collected the sterile morning urine and reduced the volume to one-tenth in a vacuum at 65° to 70°C. This he passed through a filter saturated with a 2 per cent carbolic acid solution. The filtrate was used for intracutaneous injection in small amounts and, as a control, solutions of tuberculin 1 to 1000 and 1 to 10,000 were used. A positive reaction was supposed to indicate metabolic products of active pulmonary tuberculosis. Lanz used the test in 100 surgical cases and found a negative reaction in all nontuberculous bone conditions and a positive reaction in the tuberculous bone conditions. The degree of the reaction ran parallel with the degree of activity of the process. Six cases of tuberculosis gave a negative reaction, two of congenital lues a positive reaction. Offenbacher tried the test in 20 cases of pulmonary tuberculosis, 19 of which had tubercle bacilli. Observations were made at 24 and 48 hours. Three types of reaction were observed: (1) Those that showed a definite infiltration and reddening at the site of injection (positive). (2) Those that showed no reaction at all. (3) Those that showed no reddening but had a palpable nodule (negative). Of the 20 cases of active tuberculosis only three gave a positive reaction. It is believed that a positive reaction very likely means active tuberculosis, whereas a negative reaction has no significance. *Über die Untersuchung auf Aktivität der Lungentuberkulose nach Wildbolz, R. Offenbacher, Zeitschr. f. Tuberk., September, 1920, xxxii, 355.*

Auto-Urine and Autoserum Biologic Test for Tuberculosis.—Further experience has confirmed the reliability of the test. In this communication from Wildbolz's service, Imhof states that the responses were constantly negative in the nontuberculous and (with a single exception) constantly positive whenever there was an active tuberculous process. In some of the cases there were no clinical manifestations at the time to sustain the positive biologic reaction, but the course of the cases always brought signs of active tuberculosis before long. He applied the double auto-urine and autoserum tests to 100 persons, and usually the intracutaneous tuberculin test at the time or later. The positive response is an infiltration, palpation of a lump in the tissues; redness and necrosis are disregarded. In fact, he examines for the response with eyes shut. The auto-urine reaction naturally depends on the kidneys being functionally capable of secreting; when this is not the case the autoserum answers the same purpose, but the response is never so pronounced as with the urine. Serum obtained after clotting of the blood does not elicit a response, confirming that the antigens are combined with the formed elements of the blood. He regards these auto tests as more reliable and more delicate than the findings with clinical and roentgen ray examination. To avoid disturbing protein reactions with the blood serum, he precipitates the albumin with alcohol and heating for a minute or two. When the patient is in a condition of anergy, the intracutaneous test with his urine or serum may have to be applied to another person known to be tuberculous.—*Über die Wildbolz'sche Eigenharn- und Eigenserumreaktion zum Nachweis aktiver Tuberkuloseherde, O. Imhof, Schweiz. med. Wchnschr., November 11, 1920, 1033.*

Tuberculosis of the Ear.—The delicate structures of the middle ear are most prone to be attacked by tuberculosis at the two extremes of life. If it occurs during the last stages of pulmonary tuberculosis it is of the nature of a terminal infection. The infantile type is of greater importance, as its prevention and cure may be furthered by the work of the otologist. The great majority of cases of acute otitis in infants undergo a natural cure. Chronic otitis is a rare disease of infant life, apart from tuberculosis. Duration over two months of aural suppuration in a child under one year should lead one to suspect its tuberculous nature. The onset is gradual, and, in striking distinction from acute otitis, is unaccompanied by pain. The mere presence of discharge from the meatus may be the first sign. The tympanic membrane frequently shows more than one perforation. The lymphatic glands around the ear are enlarged, and may be the seat of caseation and abscess formation. Facial paralysis is found in about 50 per cent of the cases. Middle ear tuberculosis originates probably by the passage of infection from the nasopharynx to the ear by way of the Eustachian tube, which, during early life, is relatively shorter, wider, and straighter than it is in the adult. Very probably the original seat of infection is in adenoids where histologic evidence of tuberculosis has often been found. The infection in most cases is milkborne. Operative treatment is indicated in all cases, and should consist in the performance of the radical mastoid operation. Prognosis varies according to the environment and social condition of the patient. After-treatment on sanatorium lines is of prime importance.—*Tuberculosis of the Ear, D. Guthrie, Brit. J. Tuberc., October, 1920, xlv, 164.*

Nontuberculous Complications of Pulmonary Tuberculosis.—Some patients with positive sputum present symptoms that are blamed on the tuberculous condition and which influence the prognosis and treatment greatly if discovered and remedied. It is unfortunate that many physicians, after finding bacilli in the sputum or physical signs in the chest, stop making further examination of the patient and attribute all symptoms such as fever, chills, etc., to tuberculosis. The natural course of a tuberculous infection is toward improvement and in any given case of apparent good resistance, with a continuation of symptoms after proper rest and hygienic treatment, some other focus of infection should be sought and treated. Postmortem examinations have shown that other infections may be superimposed in the lungs and be even more extensive, e.g., influenza or pneumonia. Five cases are reported. The fever in the first case was due to recurrent tonsillitis and subsided and remained normal after tonsillectomy. Abscess of a tooth accounted for the fever in the second case, which became normal after removal of the tooth. Symptoms of toxemia and irregular temperature were due to chronic appendicitis in the third case. Removal of an ulcerated appendix was followed by a fall in temperature to normal. A low hemoglobin content accounted for the shortness of breath in the fourth case. Iron was administered hypodermically and after a few doses breathing became normal. In the fifth case with irregular fever which was higher every third day, blood examination showed malarial parasites and, following eight weeks of quinine treatment, the temperature is normal. The improvement in the patients' mental attitude following clearing up of other infections is wonderful at times, and this increases resistance to tuberculous infection.—*Nontuberculous Complications of Pulmonary Tuberculosis, H. F. Gammons, Boston M. and S. J., December 9, 1920, clxxxiii, 685.*

Hernia of the Pleura Complicating Pneumothorax.—In Hale's search of the literature, he found no case even similar to the one reported. The patient, thirty-six years of age, had pulmonary tuberculosis with left, spontaneous pneumothorax. In the left back there was a semilunar tumor. It extended downward along the vertebral border of the left scapula, from a point about 8 cm. above the inferior angle, and upward and outward 9 cm. from the same angle. It was soft and compressible, though under some tension. To percussion it was resonant. It could be almost entirely reduced, only to reform when pressure was removed. Coughing hastened the filling out and caused a plain impulse. This was evidently an air-filled, hernial sac of the pleura. The patient did not feel very ill and after a few days in the ward, against urgent advice, he left before a photograph was taken. Five cases of hernia of the pleura, found in the literature, are reviewed.—*Hernia of the Pleura Complicating Spontaneous Pneumothorax, H. E. Hale, Med. Rec., January 1, 1921, xcix, 16.*

Pleurisy Due to Cold.—The patient, male, in the thirties, of athletic constitution, had been suffering from pain in the left side of the chest for a few days. Physical examination revealed left pleural effusion which on exploratory puncture proved to be hemorrhagic with partial hemolysis. The patient had been exposed to extreme cold acting directly on the left side, while rowing in January, so much so that the perspiration which had formed on the left side was positively frozen. A week after the first exploration the fluid had diminished and was less red. Shortly afterwards the patient recovered fully. The temperature never rose above 37.6° and the patient did not remain in bed during his illness. About two months later, he consulted a nose and throat specialist who took blood for a Wassermann test and found it positive. The luetic infection dated from November, 1919. The rapid and benign evolution of the effusion and the general constitution of the patient permit the exclusion of tuberculosis as an etiologic factor, though animal inoculations or roentgenograms had not been made. Syphilis is difficult to exclude. Pleurisy due to cold, rheumatism, syphilis and liver conditions are discussed.—*Un cas probable de pleurésie à frigore, C. Honoré, Liège méd., November 20, 1920, xiii, 1155.*

Tuberculous Myocarditis.—Various arrhythmias may be met with in chronic or acute pulmonary tuberculosis. Lenoble has personally witnessed one case of sinus arrhythmia, with alternating pulse; six cases of auricular fibrillation; two of nodal rhythm; three of premature beats; one of paroxysmal tachycardia with alternating pulse; one of prolongation of the *a-v* interval with alternation of the jugular pulse, and one showing secondary waves during the *a-v* interval. Fluoroscopic studies showed the heart to be sometimes small, as in the average case of tuberculosis; generally, however, it was enlarged as a whole or in one of its parts. The blood pressure ranged from 70 to 190 mm. of mercury. The prognosis is unfavorable in these cases because the heart disturbances are an expression of a deep-seated pathological change in the myocardium, superadded upon the tuberculous disease involving other organs. The existence of paroxysmal tachycardia or of nodal rhythm is particularly ominous. The diagnosis is based partly on the absence of a history of rheumatism or other major infections. Out of fourteen cases in which a Wassermann test was made, the author obtained only one positive result. The gross pathology of the heart was rather variable, but microscopic study sometimes yielded rather striking changes. Actual angiomas were found at the junction of the superior vena cava with the auricular muscle tissue. Other conditions noted included fibrosis and lime infiltration about the bundle of His, perifascicular fibrous deposits, and changes in the vessel walls. In one of the cases of nodal rhythm the node of Keith and Flack was infiltrated with small primitive connective tissue cells compressing the muscle fibres. In the other case there was in addition thrombosis of the pectineal tissues. Out of nine guinea pig inoculations, two were positive. The author recognizes not only an active type of heart muscle disease in tuberculosis, viz., bacillary myocarditis, but also a type attended with cicatricial deposits due to healed tuberculosis, such deposits being responsible for the arrhythmias observed. The connective tissue deposits, as in the case of the kidneys, need not necessarily contain tubercle bacilli. These deposits are due to the sclerosing toxins of the tubercle bacillus.—*Myocardites tuberculeuses et myocardites bacillaires, M. E. Lenoble, Bull. Acad. d. Med., October 19, 1920, lxxxiv, 151.*

Surgical Tuberculosis.—In bone and joint tuberculosis the prognosis is not unfavorable if all curative hygenic-dietetic measures can be applied. Treatment of tuberculous joint lesions in children should always be conservative. Children should not creep and play around on the unprotected floor. The tubercle bacilli get into their mouths from their hands, and get into their intestines from their soiled slice of bread and butter. It would be a good plan if we followed the example of the Orientals and put off our shoes before entering the house. As to renal tuberculosis, the mortality after nephrectomy has been constantly declining until now it is less than 4 per cent. A young man free from pathologic antecedents developed a nodule in the epididymis. He was advised to take a vacation with local and general sun baths. In three weeks the sun rays had acted like a cataplasm, lighting up the cheesy focus found in the epididymis, with perforation and fistula.—*Chirurgische tuberculose, O. Lanz, Nederl. Tijdschr. f. Geneesk., October 16, 1920, lxiv, 1511.*

Tuberculosis of Spine Resembling Pyelitis.—It very seldom happens that a lesion of the spine sufficient in extent to cause nerve pressure and therefore pain does not also produce impaired motility; yet occasionally this is the case. Also it may not be possible to induce the typical pain by jar or by posture. Since, however, the pain is produced by pressure on nerve trunks or roots, these nerves are to some extent diseased and therefore there should be and usually are present alterations of sensations, in the area supplied by the nerve, and not infrequently disturbances in the reflexes. Trophic or motor changes arise later. Due attention to the neurological manifestations of the spondylitis should prevent the error made in this case. The patient, middle-aged, had lost 50 pounds in a year and was suffering from recent attacks of unilateral pain resembling renal colic, intermittent fever and pyuria. Cystoscopic examination revealed pus from the kidney on the painful side. Examination of the spine and radiograms were negative. Nephrectomy was performed January, 1920, with resulting drop in temperature and marked general improvement. The patient returned April, 1920, with physical signs and X-ray findings of disease of the vertebra.—*Tuberculosis of the Spine Resembling Pyelitis, N. B. Foster, J. Urol., December, 1920, iv, 559.*

Nontuberculous Spina Ventosa.—Cases of spina ventosa are occasionally encountered which are not due to tuberculous lesions, being the clinical manifestations of either syphilis or a sporotrichosis infection. These morbid processes, in fact, are capable of infecting bone tissue and of determining numerous clinical types, such as hypertrophic ostitis, purulent osteoarthritis, intraosseous abscess, and ostitis of the vertebrae — sporotrichotic Potts' disease. In some cases it may offer the complete clinical picture of spina ventosa. Chevalier and Darbois have published typical cases. Usually writers who have observed and described chronic sporotrichotic spina ventosa have insisted on the absence of bone lesions and the low-grade intensity of the periostitis corresponding to this clinical phenomenon. On the contrary, in the cases described by Chevalier and Darbois the bone and periosteal lesions found by radiography fully justify the term of sporotrichotic spina ventosa, the process occurring in three different types, namely, ossifying periostitis, rarefying ostitis with decalcification with a reticulated or lacunary aspect, and intraosseous abscess. The resemblance to spina ventosa is thus complete, clinically and pathologically. Hereditary syphilis may likewise give rise to analogous types and the spina ventosa of hereditary syphilis is much more frequent than has hitherto been suspected. The lesion usually attacks the thumb and index finger, often on both hands. The radiographic findings do not differ essentially from those obtained in the tuberculous variety of the process, and the most that can be said is that there is rarely any very considerable detachment of the periosteum and that the lesions are especially those of rarefying ostitis. But the true diagnosis can be made only when other evidences of luetic taint are present and the Wassermann reaction is positive. Consequently, in all cases in which suspicion of syphilis exists a blood examination must always be resorted to. As to sporotrichosis, it has not the same predilection as syphilis and tuberculosis for young subjects and preferably attacks adult individuals. Radiograph is therefore not sufficient for making a diagnosis of the nature of spina ventosa, but it is unquestionably a very excellent auxiliary in confirming any hesitancy in diagnosis and in giving indications for proper reatment. Its usefulness is still greater when the results of radiographic treatment are to be controlled and for following the phases and progress of the process, as well as to appreciate the proper time to interrupt treatment. It must be admitted that the esthetic and functional results obtained by Roentgen ray treatment are almost always equal to those of conservative surgery, especially when the case comes under observation in its earlier phases, and in the tuberculous variety of spina ventosa advanced bone lesions with fistula are no contraindications for the treatment. Carried out with those precautions dictated by experience, the roentgen ray treatment offers no danger from the viewpoint of the integrity of the integuments or the future growth of bones. In the luetic variety a specific treatment should be instituted at the same time. *Editorial, Med. Rec., January 22, 1921, xcix, 147.*

Primary Tuberculosis of the Bladder.—Jungano reports a case in a woman of thirty-five and reviews the literature on the diagnosis and outcome. He wrote to twenty-five leading urologists to inquire their experience with primary tuberculous cystitis, and only two had ever known of an instance. One of these stated that as catheterization of the ureters had not been done, it was impossible to exclude involvement of the kidneys. Brongersma was the other, and in his case the diagnosis had been primary tuberculosis of the kidneys, but on attempting the proposed nephrectomy the right kidney was found sound. Several months later the left kidney was exposed, and was likewise found sound. The diagnosis was thus corrected to tuberculous cystitis. This patient, a woman now thirty-four, had had symptoms from the urinary apparatus since the age of ten; eighteen years have elapsed since the attempted operations on the kidneys. The general health is fair but the chronic cystitis has grown worse.—*Tuberculose primitive de la vessie, M. Jungano, J. d'Urol., x, 15.*

Genital Tuberculosis in the Male.—Barney presents among his conclusions the following which he considers of importance: (1) The epididymis is the primary focus in the genital tract. (2) It is always secondary to a focus elsewhere in the body, this focus being situated most often in the lung. (3) The prostate and seminal vesicles are invaded by the disease early and often, but after removal of the epididymis clinical cure is finally established. (4) The second epididymis becomes involved in at least half the cases, but involvement of this organ may be obviated by early resection of its vas deferens. (5) Orchidectomy is unnecessary if the testicle is free from disease, and even if affected the diseased portion can be successfully removed in many instances. Even a portion of one or both testicles is worth saving, both on account of the internal secretion and the mental effect upon the patient. After castration the sexual function may be unimpaired.—*Further Observations on Genital Tuberculosis in the Male, A. J. D. Barney, Am. J. Surg., December, 1920, xxxiv, 317.*

Tuberculosis of the Adnexa.—Three women whose tuberculous internal genitals had been removed are in perfect health now from two to three and a half years after the operation. In 4 others only one tube and one ovary had been removed, and one of the women is in good health a year later; the 3 others have all increased in weight but all have still a small fistula, two, eight and thirteen years after the unilateral castration. The fistula secretes occasionally in one, and, in another, blood oozes from the fistula during menstruation. Secondary tuberculosis was responsible for the death of 3 others. These 10 patients are the only ones that have been followed to date of a total of 28 cases of tubal or ovarian tuberculosis, with 3 deaths soon after the operation. In 3 of the women the genital tuberculosis developed from a few weeks to two months after childbirth or miscarriage. In 27 of the cases the peritoneum or adjacent organs were involved, and in 20 cases the lesions were bilateral. The genitals were involved in only one of their 55 cases of nephrectomy for tuberculosis in women, while there were 3 cases of tuberculous epididymitis in 19 nephrectomies in males.—*Quelques réflexions sur la tuberculose salpingo-ovarienne (a propos de 28 observations personelles), H. Hartman, Bergeret, and Remilly, Gyn. & Obstetr., August, 1920, ii, 3.*

Genital Tuberculosis.—In investigating the outcome in his cases of genital tuberculosis, the author has been surprised to find the women in excellent health ten years or more after operative treatment of afebrile genital tuberculosis, and even without operative intervention. But when there were fever and night sweats, the outcome was usually fatal. However, recent favorable experiences with roentgen rays and ultraviolet rays in such cases justify great hopes for the future.—*Tuberculose der vrouwelijke geslachtsdeelen, L. F. Driessen, Nederl. Tijdschr. f. Geneesk., October 23, 1920, lxiv, 1652.*

Experimental Research on Primary Tuberculosis of the Female Genital Organs.—Bauereisen injected 0.2 gm. of a bovine tubercle bacillus emulsion through an abdominal incision into the seminal vesicles of four male guinea pigs. A severe tuberculosis of the seminal vesicles, the prostate and the vas deferens developed, which extended into the epididymis, by way of the lymphatics. Tubercle bacilli were found in the bladder urine of four of the animals. There were tuberculous nodules in the peritoneum, liver, spleen and lungs. Of eleven healthy female guinea pigs laparotomy was performed on four and the cornua uteri ligated and divided. The other seven were left intact. After the wounds of those operated on had healed, the males and females were put together. Five weeks later seven of the females were killed. In four instances a typical tuberculosis of the vaginal mucosa had developed; twice an extensive tuberculosis of the cornua uteri was noted. As to direct infection of the embryo, the results were negative. However, bacilli, together with infiltration, were found in the liver of one embryo; also primary tuberculosis of the vagina; but as acidfast, that is, tubercle bacilli, could not be demonstrated, Bauereisen thinks the condition must be explained by hematogenic infection of the embryo by the mother.—*Experimenteller Beitrag zur Kohabitations tuberkulose der weiblichen Genitalien, A. Bauereisen, Zentralbl. f. Gynäkol., August 14, 1920, xliv, 905.*

Hemorrhagic Purpura and Tuberculosis.—Garin cites Schupfer's case of chronic hemorrhagic purpura with fifteen attacks in the course of fourteen years, and his twenty-six primary cases to sustain the view that hemorrhagic purpura is not a morbid entity but is merely a manifestation of some other disease. The primary disease is almost inevitably tuberculosis. In a personal case described, everything seemed to indicate a primary severe hemorrhagic purpura in a young man followed rapidly by acute nephritis which proved fatal in less than a month after the first symptoms of the purpura. Necropsy disclosed miliary tuberculosis, affecting the kidneys predominantly. The purpura, pain in the joints, etc., were merely the expression of toxic action from the tuberculosis.—*Porpora emorrhagica e tubercolosi, G. Garin, Rif. Med. October 16, 1920, xxxvi, 952.*

Tuberculous Meningitis.—The point emphasized by Libby is that severe headache of sudden onset and persistent character in an adult patient with a history of tuberculosis, either active or quiescent, should awaken a suspicion of tuberculous meningitis. And especially if taken in connection with disturbances of the motility of the eye, upper lid or pupil, or impairment of vision, this type of headache should strongly suggest tuberculous meningitis.—*Tuberculous Meningitis, G. F. Libby, J. Am. M. Ass, December 18, 1920, lxxv, 1691.*

Vaccine Therapy of Tuberculosis.—Maragliano reviews the experiences at the medical clinic of Genoa last year. Among others of special interest he reports that three tuberculous patients were given vaccine treatment and the conspicuous and progressive development of antibodies was systematically recorded. The results were as favorable as in former years in all cases adapted for active specific treatment. In one case of tuberculosis of both kidneys in particular, surprising results were realized. Teissier of Lyons has also published impressive results with the vaccine in similar cases. The vaccine is the same as that used in prophylaxis. A number of his clinically cured tuberculous patients passed through influenza without any signs of activity from their extinct tuberculosis at the time or since. For over twenty years he has been preaching that if the children exposed to tuberculosis were given systematic preventive vaccine treatment with killed bacilli, the campaign against tuberculosis would enter an effectual and positive phase.—*Lezione di chiusura al corso clinico 1919–1920, E. Maragliano, Rif. Med., July 17, 1920, xxxvi, 641.*

Tuberculin Treatment for Children.—Failure of tuberculin treatment is probably due to inability to determine the appropriate dose for the individual patient, which may be one-millionth of a milligram in one patient and one-tenth of a milligram in another of apparently the same type, owing to wide differences in tuberculin hypersensitiveness and tuberculin tolerance. The usual method of giving all patients practically the same initial dose does harm to those who should take less and is ineffectual in those who require more. The correspondence between tuberculin hypersensitiveness and tuberculin tolerance suggests the determination of the therapeutic dose for each patient as the amount of tuberculin that gives the minimal reaction when injected into that patient subcutaneously. In order to test the patient's sensitiveness to tuberculin, the following test is made: Intracutaneously in a patient's forearm at the same time, one ten-millionth of a milligram is injected distally, one-millionth of a milligram medially, and one hundred-thousandth of a milligram proximally, the injections being made in a diagonal line. If no reaction occurs after twenty-four and forty-eight hours, one ten-thousandth, one-thousandth and one-hundredth milligram are later injected into the other arm. If still no reaction occurs, one-tenth of a milligram and 1 mgm. are injected, and, if necessary, still later 10 mgm. The smallest dose that produces a distinct reaction is administered therapeutically, either by mouth or subcutaneously. If this dose produces a favorable reaction, increase of appetite, reduction of temperature, it is repeated every three or five days, until it loses its effect, whereupon it is gradually increased until it again produces a favorable reaction. If the tuberculin seems to produce no effect at all, it is still repeated for several weeks and then increased. At intervals, tests for sensitiveness are made by injecting intracutaneously the dose the patient is receiving, and doses one-tenth and ten times that amount. If no reaction occurs from any of these, one hundred times one thousand and ten thousand times the amount the patient is taking are injected. If the amount producing the intracutaneous reaction is greater than the amount being given therapeutically, the latter is increased rapidly until it corresponds with the former. The usual rate of increase is about 50 per cent. The tuberculin given is the T. R. It was found that it made little difference whether the tuberculin was given by mouth or subcutaneously. The author gave the tuberculin treatment seldom or never to patients who were doing well without it. The success of this method in children was demonstrated in 19 cases at the Eagleville Sanatorium, Pennsylvania. The initial doses varied from one hundred-millionth to one-hundredth of a milligram and were increased ten times to one hundred and twenty thousand times over periods from one to twenty-one months, practically without producing an unfavorable reaction. A large proportion showed improvement in general condition, reduction of temperature and gain in weight. —*A Method of Determining the Appropriate Dose of Tuberculin for the Tuberculous Child, M. Solis-Cohen, Arch. Ped., November, 1920, xxxvii, 641.*

The Martinotti Vaccine for Tuberculosis.—Out of 27 cases treated with the Martinotti antituberculous vaccine, some of which were kept under observation for a period of three years, 19 were completely cured. The first signs of improvement were an increase of appetite and an unusual sense of well being. These subjective symptoms were supported by objective signs. The cough and night sweats diminished rapidly, the weight increased, the temperature returned to normal, the respirations became less frequent, râles disappeared, the sputum became thinner, the tubercle bacilli granular and shorter and finally disappeared, and the pulse was stronger and less frequent. On the X-ray plate, the shadows of infiltrations became less intense and more circumscribed, indicating progressive scar formation. Under the fluoroscope, the diaphragm invariably resumed its motility.—*Contributo clinico alla terapia della tubercolosi polmonare col vaccino antitubercolare Martinotti, E. Ruggeri, Tubercolosi, June, 1920, xii, 169.*

Spengler's Immune Bodies.—Borgogno used the immune bodies in his dispensary at Alessandria in three types of patients: those with closed lesions, those with open lesions, but in fair general condition, and those with open lesions of a serious nature and with signs of toxemia. The immune bodies were prepared in dilutions graded according to the stages of the disease. The far advanced cases received the most dilute solutions by hypodermic injections every two or three days in increasing doses. No reactions other than a slight rise of temperature were noticed. The advanced cases were not at all benefited, contrary to the experience of Hollós. The milder cases, however, improved, especially those with closed lesions. They gained in weight and lost most of their subjective symptoms. No other treatment was given during the administration of the immune bodies, and the patients remained at their work.—*I corpi immunizzanti di C. Spengler nella terapia antitubercolare, M. Borgogno, Tubercolosi, April, 1920, xii, 109.*

Allergy or Anergy.—Those free from tuberculosis do not react to the largest doses (20,000 mgm.) of tuberculin; they are truly anergic. This would suggest that tuberculin therapy should aim at rendering patients anergic. The experience during the war seems to prove the correctness of this theory. Former patients who had been rendered anergic did not relapse while a very large number of those who had remained allergic did relapse. Many, still allergic at the time of entering military service, became anergic in the course of time. Anergy is not necessarily the result of "biologically concluded" tuberculin therapy but rather the result of healed tuberculosis. In all his practice Krämer has never seen relapses after tuberculin therapy carried out to its biological conclusion (anergic state). Further observation must show whether patients rendered anergic by tuberculin therapy are permanently cured.—*Ist die Allergie oder die Anergie der Tuberkulösen das Nützlichere für den Kriegsdienst?, C. Krämer, Beitr. z. Klin. d. Tuberk., August, 1916, xxxvi, 57.*

Tuberculin Treatment.—A review of current opinion in different countries since Koch's publications on tuberculin treatment. Thirty years have elapsed, but no common opinion has been established upon the value of its use. In every country friends and enemies of tuberculin are still found; all grades of indifference or enthusiasm occur. Bandelier and Roepke are still admirers, while Schröder claims to see the same good results without tuberculin treatment. The French authors are divided in the same way: Jeanneret wanting to put tuberculin in the hands of all practitioners, Jousset considering its application dangerous, illogical and absurd. England and America show the same picture of divided interest. Pathologists like Virchow warned against the focal reaction in tuberculosis. Tendeloo admits the possibility of favorable outcome after focal reactions. The weak point in its application remains the impossibility of estimating the amount of good (or harm) different foci in the lungs will receive from reactions. In chronic pulmonary tuberculosis older and younger foci exist. It seems unreasonable to expect favorable results in the ordinary case of pulmonary tuberculosis on account of the pathological changes. The experience of different sanatorium men both in Europe and America indicates that patients do not lose their bacilli more easily when treated with tuberculin, notwithstanding Bandelier and Roepke's enthusiasm. Bardwell's statistics seem illuminating on this point. The results of the author are the same as those obtained by H. M. King, analyzed by Waters of Loomis, N. Y. Best results may be obtained perhaps in cases of pulmonary tuberculosis with a tendency to healing, without bacilli, where the pathological changes are nearly identical and where the risk of dangerous focal reactions is small. Laryngeal tuberculosis complicating pulmonary tuberculosis does not seem to improve under tuberculin treatment. Tuberculosis of the eye seems often to improve under specific treatment. X-ray treatment has replaced tuberculin in cases of tuberculous glands and so called surgical tuberculosis, though some cases may do well under tuberculin treatment. Tuberculin should not be given according to a schedule; individualization is necessary. The skin reaction carried out cutaneously or intracutaneously may give some clue as to the power of resistance to tuberculin. This however is not the same as resistance against the disease. The original studies of Deycke and Much, and Altstaedt and others sufficiently indicate this. It remains to be seen whether the partial antigen treatment will be more successful. Its use will be limited at its best. Its application will cause a good deal of inconvenience to the patients; and not much satisfaction can be expected from tuberculin treatment in pulmonary tuberculosis of children, notwithstanding Jeanneret's interesting work on the intracutaneous method. Petruschky's application of tuberculin as a prophylactic measure and Von Leube's advice to treat children with tuberculin who show a positive skin test do not seem suitable for general application. The problem of resistance against tuberculosis is not solved by tuberculin treatment.—*Tuberculin Treatment, P. J. L. de Bloeme, Nederl. Tijdschr. v. Geneeskunde, September, 1920.*

Operation for Tuberculosis of the Wrist.—The operation devised by Ely necessitates cutting a groove in the radius and the third metacarpal and transplanting into it a graft from the tibia. The result is said to be a useful hand, possessing as much rotation as before the operation, and with excellent power in the fingers and thumb.—*An Operation for Tuberculosis of the Wrist, L. W. Ely, J. Am. M. Ass., December 18, 1920, lxxv, 1707.*

The Internal Use of Iodine.—In 1914 Boudreau made the statements: (1) Iodine is a direct specific against tuberculosis. (2) It should be administered in moderate doses, gradually increasing to the point of tolerance. The term iodism should be changed to iodurism, that train of symptoms caused by the administration of the iodides, rather than iodine itself. Relatively enormous doses of the tincture of iodine, up to 150 drops a day, can be tolerated if well diluted. Boudreau claims excellent results in pulmonary tuberculosis even without the rest cure. This tolerance for iodine has also been noted by English physicians in cases of rheumatism. Dufour has tried iodine in the treatment of pulmonary tuberculosis but without encouraging results. He claims that in large doses this drug is the best means of treating adenitis.—*L'usage interne de la teinture d'iode à hautes doses, L. Cheinisse, Presse Méd., September 25, 1920, xxviii, 678.*

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Abstracts should be sent typewritten on one side of the page only. They should be as concise and compact as the subject matter of the article warrants. They should be headed with a short title, and followed by the full title of the paper, author's name, journal, date, volume and page.

Editor's Note: See p. 142, January, 1921. **Review,** ***vol. iv, no. 11, Abstract Section. There is here printed verbatim an editorial from the*** **Medical Record,** ***November 20, 1920, xcviii, 862, entitled The Kidney in Pulmonary Tuberculosis. Although the author's name is not mentioned this editorial is a literal translation of the Conclusions of a very meritorious thesis by Dr. M. L. Kindberg on Études sur le rein des tuberculeux, Paris, G. Steinheil, 1913. We take pleasure in acknowledging its source, which has been brought to our attention by Dr. Kindberg.***

Mercury Compounds in the Chemotherapy of Experimental Tuberculosis.—This report concerns the bacteriostatic and therapeutic effect of 24 inorganic and organic compounds of mercury on the human tubercle bacillus and on experimental tuberculosis in guinea pigs. All the compounds showed some inhibitory power, nearly all inhibited growth completely at 1:10,000, many also inhibited at 1:20,000. In allyl alcohol mercuric acetate, double salt of methylene blue and mercuric chloride and l-amino, 2 (paranaphthalin azopenyl mercuric acetate) 5 sulphonic acid, the bacteriostatic action went further than 1:20,000. As to the chemotherapeutic experiments, as compared with the untreated controls that had been inoculated with the same dose of the same strain of tubercle bacilli, several treated guinea pigs showed a greater duration of life and less extent of disease. The drugs producing this action were methylene blue and mercuric chloride, mercurous chloride, mercury potassium cyanide, mercuric succinimide, mercury phenolphthalein, methylene green and mercuric chloride, diazo amino methylene blue o-phenol mercuric chloride. In nearly all of the animals tested, the infection was due to a strain of low virulence, and when the same drug was tested with a strain of high virulence no effect was noticed. Only in the case of a set of animals treated with the double salt of methylene blue and mercuric chloride and with a set treated with diazo amino methylene blue o-phenol mercuric chloride has there been a similar beneficial effect on animals inoculated with a virulent strain, and the effect of none of these drugs was such that the disease could be called cured. Since the guinea pig is far more susceptible to tuberculosis than is the human being and responds to infection with a more rapidly progressive and fatal disease than does man, a drug that has a decided beneficial effect in the guinea pig would probably have a much greater effect in man.—*Mercury Compounds in the Chemotherapy of Experimental Tuberculosis in Guinea Pigs. I, Studies on the Biochemistry and Chemotherapy of Tuberculosis. XXI, Lydia M. DeWitt, J. Infect. Dis., February, 1921, xxviii, 150.*

Light Therapeutic Studies with Furstenau's Actinometer.—On the ground that X-rays are wave lengths of light which can be measured, Fürstenau was led to study selenium cells as a means of measuring quartz light radiations. He finally brought forth his actinometer. The methods of Bordier, Stumpke and Bering and Meyer are too difficult to employ in daily practice. The variations in light emitted from a Bach's alternating current mercury quartz light with and without resistance coils are shown, demonstrating how necessary it is to carefully measure the intensity. Graphic charts are required to show accurate results. Differences of 300 per cent during the burning period of one hour were shown for similar burners. The amount absorbed by various films can also be studied. The uviol film was seen to absorb 30 to 40 per cent. Further studies are being made, especially in regard to the amount of warmth in lamps which varies a good deal in the same type. It seemed best to eliminate the rheostat resistance in order to take advantage of the greatest amount of electrical energy; however it is best to correspondingly increase the distance of the source of light from the patient. With Bach's "Höhensonne" and its reflectors, the law that the light intensity varies inversely with the square of the distance does not hold. A lamp with an old burner showed only one-half the intensity that it did with a new burner. The apparatus opens up a large field for study.—*Lichttherapeutische Studien mit dem Fürstenau-Aktinimeter, F. Meyer, Münch. med. Wchnschr., December 3, 1920, xlix, 1410.*

The Quartz Laryngeal Mirror.—The ultraviolet rays seem to be the most important for therapeutic use in laryngitis; the greatest possible intensity is desired. With glass laryngeal mirrors marked absorption and loss occur, both for the incident and reflected light. With quartz, practically none is lost, due to the absence of absorbing power. It is to be preferred for other reasons also: it does not oxidize as metallic mirrors do, is not destroyed so soon, resists boiling and is therefore easily sterilized and not quickly scratched. This quartz mirror needs little protection as the quartz is ceramically united to the mirror deposit; the quartz can if necessary be surrounded by only a closed ring without any use of screws. In addition to this, the physician can add ultraviolet rays by reflecting with a quartz head-mirror, into the pharynx and larynx. Noll's mouth adjuster is also a good addition.—*Der Quarz-Kehlkopfspiegel, H. Ladebeck, Münch. med. Wchnschr., December 10, 1920, l, 1442.*

Radiating the Larynx with Ultraviolet Rays.—The healing power of sunlight is probably due chiefly to the ultraviolet rays. The effect of these in strong dosage upon the larynx is so far not properly shown because of the lack of suitable apparatus. The quartz lamps of Bach, Kromayer and Jesionek furnish powerful ultraviolet radiation. The apparatus here offered allows easy application without the need of the patient holding the mirror, after it is once properly adjusted; the doctor's hands are also free. It consists of an adjustable mouthpiece to keep the mouth widely open and an additional holder to grasp the steel end of the laryngeal mirror. The physician fixes the apparatus so that the mirror is properly placed over the larynx and the rest is left to the patient. With ball-valve joints, most parts are freely movable. The use of Bach's quartz lamp with this is not very simple but is yet possible. It is better to use Ladebeck's quartz mirror in place of the ordinary glass laryngeal mirror. Therapeutic technic will be considered later.—*Ein neuer Kehlkopfbestrahler zur Behandlung mit ultraviolettem Lichte, F. Noll, Münch. med. Wchnschr., December 10, 1920, l, 1441.*

Dosable Light Therapy.—Just as in roentgen ray therapy, so with light, one of the most important considerations is exact dosage. Thus far, without any suitable, easily handled apparatus, light treatment is carried out in a most unsatisfactory way. No accurate comparisons between various workers and their sources of light and their results can be made. As a result of long study, in conjunction with a co-worker, Eppens, this actinometer was constructed. It consists of two parts, the first being a receiving apparatus to catch the light rays, this joined by a connecting wire of over a metre in length, with the second part, a measuring instrument with indicators and a scale. The whole is placed on a support against the wall. The receiver, containing light-susceptible selenium cells is opened by a valve arrangement to receive the light rays. The light rays change the electrical resistance of the selenium cells, and the amount of this change is determined by the quantity of the affecting light. In turn, as a result of this change, the measuring instrument records the effect in light units. The opening of the receiver to the rays of light is immediately registered on the scale. The empirical unit has direct biological relationship with the amount of light that has been shown to produce changes such as erythema, etc., on patients. By this means, light should be able to be dosed properly and will then assume a firmer basis.—*Dosierbare Lichttherapie, R. Fürstenau, Deutsche med. Wchnschr., December 2, 1920, xlix, 1362.*

The Treatment of Surgical Tuberculosis with X-ray.—There is very little uniformity of opinion in regard to X-ray treatment except in relation to the results in glandular tuberculosis. In the other types, authors are for or against it according to their past experience. The cases were not selected but all types of surgical tuberculosis were radiated and no doubtful ones were reported upon. The healed cases were termed so, only if they showed no pathologic subjective or objective findings. Of 57 healed cases, there were 50 or 89 per cent which were afterward studied for a period of four years after discharge. The author decided to use the smallest doses possible and have large intervals between. No general rule could be followed but it was necessary to individualize by noting the effect of the first dose. If abscesses were present at the start, they were punctured and often filled with iodoform in glycerin before they were radiated. The organization resulting from treatment should go hand in hand with the slight softening that must result. The effect of the radiation through irritation is to stimulate scar tissue. The action of X-rays was carefully studied by roentgen pictures. In this way foci, which were formerly indistinctly outlined, gradually assumed a sharp demarcation. The granulation tissue disappeared promptly, but the filling in of bone spaces might take years. The radiation seemed to act favorably on bone disease; of 23 cases of joint tuberculosis 13 healed completely with return of function, three with a slight loss of function and seven with ankylosis. Together with radiation, constitutional treatment was carried out. Artificial light was also employed but was not considered as favorable as sunlight. It was most important to carry out exact orthopedic principles. Extension bandages served an important function. The technic used was exposure at a distance of 26 mm. with aluminum filters of from 1 to 4 mm. thickness. The dose was 5 X of a ten-minute exposure at intervals of three to four weeks, but this was varied according to the type of disease, exposure going up as high as 25 X. Conclusions: In glandular tuberculosis, excellent results were obtained almost without exception. No operative procedures are necessary except an occasional puncture. Investigations covering thirty-seven and a half months after exposures show only 1 case with a residue. The radiations covered a period of over six months. Twenty-three hip joints were radiated, 14 of which were closed, and 13 healed. Of those with tuberculosis of the foot, only 50 per cent recovered. With elbow joints very favorable results were had, only 1 case out of 6 resisting treatment. Results were still better in disease of the joints of the hand in which all 5 cases healed. One case of sternal and spinal tuberculosis and 4 of peritoneal tuberculosis with disease of caecum healed completely. Of 40 joint cases, 33 or 82 per cent recovered. Still X-ray treatment is only an adjuvant; general constitutional treatment has to be carried out most carefully. Best results are had with children. Adults are not so favorable. X-ray radiations give better results than operation except in older patients in whom the prognosis is very doubtful.—*Über die Behandlung der chirurgischen Tuberkulose mit Röntgenstrahlen, K. Stromeyer, Deutsche med. Wchnschr., May, 1920, 514, 542.*

Heliotherapy in Surgical Tuberculosis.—Negri does not hesitate to assert from his six years of experience that surgical tuberculosis can be cured in all its forms, at every stage and at all ages with heliotherapy. He is not so affirmative in regard to visceral tuberculosis, but cites a number of remarkably successful cases from his own and Rollier's experience. Success is especially frequent in tuberculous peritonitis. In one case of tuberculous adnexitis the local and general condition improved notably during a three months' course of heliotherapy, notwithstanding a coexistent respiratory tuberculosis. But in this, as also in a case showing great improvement of a tuberculous urinary process, the patients would not wait to complete the course. He refers further to Rollier's success with tuberculosis of the testicles, adding that the practically invariable involvement of the seminal vesicles and prostate forbids surgical treatment. While all physicians admit theoretically the usefulness of heliotherapy for so called bone and joint tuberculosis, yet comparatively few insist upon it for their patients, and still fewer apply it. It is not enough to order the patient to take sunbaths. The course must be systematically planned and applied, and for this Negri urges multiplication of inexpensive institutions for the regular application of heliotherapy. His own work was done in the Novara foothill district in northern Italy.—*Elioterapia e tubercolosi chirurgiche, L. Negri, Policlin., November 15, 1920, xxvii, Surg. Sect. No. 11, 352.*

Radium Treatment of Tuberculous Adenitis.—Radium is not to be advocated as displacing surgery but its adoption is encouraged wherever indicated. Of 32 cases treated during four years 27 were arrested and apparently cured, 3 disappeared and 2 showed recurrence. One died two years after treatment from pulmonary tuberculosis. Following a massive application of radium over an area of infected glands, a general average dosage being 200 mgm. for twenty-four to thirty hours, the improvement is marked. As a rule the masses do not completely disappear, but they become inactive and reduced to small dense nodules. Sinus formations are successfully treated by advancing a tube of radium well up into the top of the sinus. Three cases are reported where the radium treatment has been successfully employed in tuberculous adenitis in adults.—*Radium Treatment of Tuberculous Adenitis, C. E. Field, Long Island M. J., November, 1920, xiv, 424.*

Mechanical Treatment of Tuberculosis.—The following types are suitable for pneumothorax treatment: Cases of severe, massive hemoptyses where it is definitely known from which lung the hemorrhage arises, cases of small or moderate hemoptyses recurring in spite of all less radical measures, unilateral active ulcerative lesions which, regardless of rigid rest and the proper dietetic-hygienic regimen, progress steadily. Contraindications are bilateral active processes, the simultaneous presence of severe disease of the cardiovascular-renal system, diabetes and active intestinal tuberculosis. The gases used are nitrogen, oxygen and sterile atmospheric air. The operation itself is comparatively simple. Strict asepsis is essential. Under carefully applied local analgesia no suffering and little inconvenience need be experienced by the patient. The site for injection favored by most workers is in the fifth or sixth interspace in the anterior axillary line. Except in cases of severe hemoptysis where large quantities (1200 to 1500 cc.) of air may be used to effect speedy complete compression, a course of treatment is ordinarily initiated by the employment of small quantities of air, 200 to 300 cc. to begin with, followed by 300 to 500 cc. two days later. The refills may be spaced from one to four weeks apart depending on the rapidity of absorption of the air. Clinical recovery long precedes complete anatomic recovery. Most workers agree that at least two years are needed; some cases require a much longer period, depending upon the extent and type of lesion, the patient's general responsive powers, and his reaction to environmental and occupational stimuli. If after two years a patient is able to do one-half day's work and remains free from clinical evidence of activity, structural cure has been realized and the lung is permitted to reëxpand. The general results of pneumothorax therapy are encouraging. The lives of patients have in many instances been greatly prolonged; a fair percentage have been restored to usefulness; a small percentage have become apparently permanently cured. Yet these are all cases which would otherwise most likely have proceeded to fatal termination.—*The Mechanical Treatment of Tuberculosis, F. Murray, Long Island M. J., November, 1920, xiv, 417.*

Postural Rest for Pulmonary Tuberculosis.—Excellent results have been obtained in more than 200 patients with tuberculosis who were subjected to postural rest as a means of treatment. At the same time, so little attention has been given to the subject by those who specialize in pulmonary tuberculosis, that the authors feel warranted in again discussing this subject. The failures encountered have been in patients either too far advanced with bilateral disease, or in those considered favorable for the application of this procedure, but who failed to carry it out faithfully. Pulmonary tuberculosis is usually in its early phase a disease of the upper lobes, and the movement of these lobes is easily controlled by postural rest. As a matter of practical experience, it has not been noted that postural rest, with the preliminary increased excursion of the diaphragm, brings any disaster to patients when the disease has involved the lower lobe. Usually when such a phase of the disease is reached, pleural adhesions are likely to prevail, and these possibly modify the motion of the diaphragm. In the normal person there is little hyperemia of the dependent lung during sleep. In a tuberculous patient, a moderate degree of hyperemia is produced by prolonged rest on the affected side. Certainly such prolonged rest does naturally assist in the moving over of the heart and of the mediastinum to the side of the more diseased and dependent lung. In patients with much expectoration, a short time several times a day is allowed to be spent lying on the less affected lung. This accelerates drainage. The patient then turns on the side of the more diseased organ, beginning with only a few minutes and gradually increasing the time until twenty hours or more a day are spent lying in this position. A small pillow is often placed under the ribs to increase the splinting effect. Results are obtained in a few weeks by the application of this thorough rest which are comparable to those obtained more quickly by artificial pneumothorax. Fever will subside, cough will cease, and sputum of many ounces may decrease to a mere trace. It has been of special interest to note the decrease and at times almost complete disappearance of râles. Many patients, considered as certainly requiring the application of artificial pneumothorax, have been restored to health by this simple procedure.—*Postural Rest for Pulmonary Tuberculosis, G. B. Webb, A. M. Forster & G. B. Gilbert, J. Am. M. Ass., March 26, 1921, lxxvi, 846.*

Multiple Fluid Collections in Therapeutic Pneumothorax.—Careful observation of 32 cases of hydropneumothorax disclosed the presence of multiple fluid collections in 5 cases. This condition could not be detected without the aid of the X-ray, which showed characteristic multiple fluid levels. Two or more independent hydropneumothorax pockets may be produced as a result of attempts to induce pneumothorax at different levels of the chest or a localized spontaneous pneumothorax may occur adjacent to a pocket of artificial hydropneumothorax. This condition is most commonly caused by pleuritic adhesions which spread out in hammock-like fashion from the visceral pleura across the pneumothorax area to the chest wall. These adhesions may be present before the induction of the pneumothorax and may occasionally be the result of a thickened interlobar septum, or they may be newly formed as a result of organization of the exudate. The coexistence of a fluid-containing cavity with a hydropneumothorax may also give rise to multiple fluid levels.—*Multiple Fluid Collection in the Chest in the Course of Therapeutic Pneumothorax, B. Stivelman and J. Rosenblatt, Am. J. M. Sci., February, 1921, clxi, 229.*

Therapeutic Pneumothorax in Exudative Pleurisy.—In summarizing the advantages of therapeutic pneumothorax in exudative pleurisy, the author emphasizes the following points: 1. It is possible to get rid of all the accumulated liquid. 2. There is a tendency to rapid healing, and there is seldom a renewal of the exudative process. 3. The formation of new adhesions and any extension of existing ones are prevented. 4. Pain due to the contact of the two inflamed surfaces is relieved by their separation by gas. 5. Thoracic shrinkage is counteracted. 6. The danger of rapid decompression is minimized. 7. Laceration of the pulmonary parenchyma, even in advanced cases, is made less likely. 8. Concomitant tuberculous lesions can be arrested. 9. The pneumothorax assists in diagnosis and prognosis. —*Il pneumotorace terapeutico nelle pleuriti essudative, V. Rustichelli, Tubercolosi, October, 1920, xii, 301.*

Bilateral Artificial Pneumothorax.—Bilateral artificial pneumothorax can effectively cure pulmonary tuberculosis. The healed lung may reëxpand and resume its normal function. The pleura may remain pervious to the same extent as before treatment, notwithstanding a long period of compression. Thus, it is possible to renew the treatment in case of a relapse. A pneumothorax may be induced in the other lung, if a lesion should eventually break out there. —*Pneumotorace artificiale consecutivamente bilaterale, G. Feldman, Tubercolosi, August, 1920, xii, 229.*

Treatment of Early Pulmonary Tuberculosis.—Pulmonary tuberculosis should not be accepted as the final diagnosis to the exclusion of all others. Other conditions may be present and must be corrected, such as diseased tonsils, obstructed nostrils, bad teeth, pelvic disorders, chronic appendicitis and gastrointestinal disturbances. Marcley emphasizes the need of medical supervision and an intelligent coöperation on the part of the patient. Open air while of prime importance is to be considered only in connection with the other elements of treatment. Change of climate has psychic as well as physiological effect. A low altitude and a long cold winter may require special consideration with some patients. The early cases as a rule do best in a rigorous climate. The importance of rest cannot be emphasized too strongly. It is impossible to lay down any rule for rest or exercise in all cases. Patients who are put to bed having only slight rise in temperature and pulse rate are allowed to walk to the toilet and to sit up for meals. Exercise is to be dosed out cautiously. On a well-balanced nutritious diet the patient makes slow gradual gain back to his normal weight. Hydrotherapy should be carefully suited to each individual. Tuberculin in selected cases if properly given proves beneficial. The treatment of tuberculosis in childhood requires a longer period of watchfulness after apparent recovery. The sanatorium is the place par excellence where the treatment should be taken, and where the patient should remain long enough to become accustomed to the routine so that he can continue the treatment after discharge from the institution under home supervision.—*Treatment of Early Pulmonary Tuberculosis, W. J. Marcley, Minnesota Med., February, 1921, iv, 96.*

The Care of Moderately Advanced Pulmonary Tuberculosis.—A hospital for tuberculous patients may be so placed within or near our cities as to insure comparative freedom from contamination of our densely populated centers and yet not so far removed that the frequent visits of relatives and friends become a hardship. This social intercourse is an important element in maintaining the morale of these patients. For ward beds, semiprivate and private rooms with nursing, medication and medical services in a private hospital as described by the author, terms range from nothing to $30 per week. The number of people suffering from pulmonary tuberculosis is being steadily reduced. A hospital for moderately advanced or far advanced patients has a large field of usefulness apart from that of the sanatorium. Symptomatic treatment and artificial pneumothorax when used persistently and intelligently are of great help to the patient.—*The Care of the Patient with Moderately Advanced Pulmonary Tuberculosis, T. A. McGoldrick, Long Island M. J. November, 1920, xiv,* 427.

The Treatment of Grave Cases of Pulmonary Tuberculosis with Partial Antigens.—Conclusions: 1. Partigentherapy may favorably influence the course of the disease even in severe cases as evidenced by the general amelioration of the condition, of physical signs in the lungs, loss of fever and increase in weight. 2. In the more difficult cases the intracutaneous method should be used. 3. The intracutaneous reaction gives many valuable indications of the progress of the disease while under treatment but should be considered only in conjunction with the clinical findings.—*Die Behandlung schwererer Fälle von Lungentuberkulose mit den Deycke-Muchschen Partial-Antigenen und die Bedeutung der Immunitäts-Analyse bei der Behandlung derselben, H. Schults-Tigges, Ztschr. f. Tuberk., October, 1920, xxxiii, 26.*

Sanatoria for Surgical Tuberculosis.—Since the war, tuberculosis has been on the increase in Switzerland, as it has in other countries, but the antituberculous work done so far has been almost exclusively directed against pulmonary tuberculosis. While eleven Swiss cantons possess each an establishment destined for the treatment of pulmonary cases, there exists at present only one altitude sanatorium for surgical tuberculosis, namely, the one that was put up two years ago at Leysin by the Vaudoise Antituberculosis League, and nevertheless, according to the statistics of de Quervain and Hunziker, there are no less than 3000 surgical tuberculosis cases per annum in Switzerland. This is evidently a great social injustice that should now be rectified and this has been undertaken by Prof. de Quervain of Berne and Dr. Rollier of Leysin. Since surgical tuberculosis is, like the pulmonary process, a disease in which the question of soil plays an active part, it is essential to place these patients in the best possible conditions for defense of the organism. An experience of twenty or more years has allowed both Bernhard and Rollier to prove that a mountain suncure fulfills these conditions perfectly, because it affords the most efficacious general treatment, while heliotherapy, combined with rational orthopedic treatment, is for many cases the best local treatment. Switzerland, with its numerous Alpine and subalpine resorts, is better placed than many other countries for organizing an antituberculosis fight for surgical cases of this affection. The advantage of mountain resorts resides in the fact that solar radiation is there most intense and continuous and patients can benefit from the sun during the entire year, an essential factor in the cure. The ideal solution would be that each canton should have its own sanatorium for surgical tuberculosis in a chosen altitude resort. In the case of small cantons several might use the same establishment. It is not a question of building luxurious installations, as at present the cost makes any such undertakings out of the question, but while waiting for better times to come, it is possible to use already existing hotels that have been little frequented since the war and which could be bought or leased under advantageous conditions, and could be altered over into hospitals. The experience gained by the free clinics at Leysin shows that such a transformation is easy to realize. It is important that the sanatoriums for surgical tuberculosis should be independent of those for pulmonary tuberculosis already in existence. The treatment of the surgical cases requires special medical knowledge, not only of heliotherapy but also radiodiagnosis, radiotherapy, orthopedics, and conservative surgery, all of which are precious adjuvants to the solar cure. An organization for occupational cure must be carried out in these establishments. Experience gained in this domain among the Swiss tuberculous soldiers quartered at Leysin allows one to conclude this is a therapeutic, physical, and moral factor of the first importance. It has also the advantage of giving patients the faculty of partially helping toward the cost of their treatment.

In order to maintain and consolidate the cure of tuberculous subjects, it is necessary that when once recovered, they should live in good hygienic conditions. By creating in the plains agricultural, market-gardening, and wine-growing colonies for convalescents, the latter can avoid returning to trades, often unhealthy, or returning to insanitary lodgings. Thus, it may be possible to solve the double social problem: on the one hand, to prevent recurrences, on the other to furnish the nation with labor, which has become progressively scarcer on account of the movement from the country to cities. In order to solve the financial side of the problem, a popular movement will be started in favor of patients with surgical tuberculosis. An appeal to the good sense of the Swiss people will not fall on deaf ears, and the funds collected will be placed at the disposal of the cantonal leagues. The above propositions propounded by de Quervain and Rollier are being examined by the Swiss Association for Tuberculosis and will undoubtedly be favorably acted on. Although the treatment of already existing surgical tuberculosis appears as an urgent necessity, it is no less important and certainly easier, to organize a prophylactic fight against these affections. Like pulmonary tuberculosis, the surgical forms almost invariably follow a tracheobronchial adenopathy—this first manifestation of tuberculous infection in childhood, so that it is important to arrest further progress of the disease by placing children in the most favorable conditions for organic resistance. This can be accomplished by the introduction of reforms in the hygiene of tenements and schools, in which a larger place should be given for the physical development of the children—schools built in the open and freely exposed to the sun. Such is the present program which is under consideration.—*Letter from Geneva, Med. Rec., February 26, 1921, xcix, 362.*

Results of Surgical Treatment of Pulmonary Tuberculosis.—Quoting from Sauerbruch, Naegeli states that of 381 patients operated on, 134, or 35 per cent, have been cured to the extent that for at least a year and a half after the operation they have been free from fever, present negative sputum and are able to perform their regular daily work. They were for the most part severe cases, resistant to internal, dietetic treatment for many years, cases that on account of large cavities and copious expectoration were especially dangerous as sources of infection. Naegeli reviews the outcome with the various methods of surgical treatment employed in recent years—among others, artificial pneumothorax; extrapleural thoracoplasty, which is to be considered if adhesions make artificial pneumothorax impossible; paravertebral resection (Sauerbruch), which consists of a more or less extensive resection of the first to the eleventh rib; filling the lung cavities with paraffin (Baer); resection of the cartilage of the uppermost ribs on the ground that ossification of this cartilage has brought about a narrowing of the upper thorax aperture (Freund); and other methods of less established value. The results of surgical treatment of pulmonary tuberculosis (which, of course, is indicated only if other measures have been persistently tried and have failed) have been very gratifying.—*Die chirurgische Behandlung der Lungentuberkulose, T. Naegeli, Therapeut. Halbmonatsh., September, 1, 1920, xxxiv, 461.*

Intracutaneous Tuberculin Treatment.—Sahli inaugurated the multiple inoculation of tuberculin with his *Nadelschnepper*, and states that this is proving in many hands a convenient and effectual method for tuberculin treatment. The large number of pricks multiplies the areas for absorption, while patients do not shrink as much from it as from a subcutaneous injection. But he now prefers intracutaneous injection of tuberculin as an improvement over all other methods. This allows greater precision in the dose, and the local reaction to the tuberculin generates local production of antibodies, which aid in immunizing. It has further the advantage that the local reaction is an index of the degree of immunization that has been realized and a guide to the dose of tuberculin to use to avoid injurious effects, as the skin seems to be far more sensitive to tuberculin than all other tissues. He emphasizes that intracutaneous tuberculin treatment and prophylaxis belong to the general practitioner, as he sees the cases in the earlier stages when tuberculin treatment offers the greatest chances for success.—*Über Tuberkulinbehandlung mit besonderer Berücksichtigung der Intrakutanbehandlung, H. Sahli, Schweiz. med. Wchnschr., July 1, 1920, l, 557.*

Immunization By Nonvirulent and Nontoxic Living Tubercle Bacilli.—Inoculations with dead bacteria do not afford complete security against infection, though they render the illness a mild one and shorten its duration. The use of living disease germs remains as the most rational method of treatment, and many attempts have been made to eliminate the dangers naturally associated with this method of treatment. The aim must be to make use of attenuated disease germs which still retain the capacity to produce immunity. Attempts in this direction, however, have encountered the greatest obstacles, although the most diverse methods of attenuation have been tried. No vaccines of great practical importance were obtained until among the tubercle bacilli of cold-blooded animals those of the turtle became the centre of interest. They occupy a position intermediate between the cold-blooded and human tubercle bacilli, on which account they are especially suited for use in the therapy of tuberculosis. They develop vigorously at 98.6° F. When cultivated at the ordinary incubator temperature they exhibit the same cultural features as human bacilli. The original strain of the tubercle bacillus of the turtle which is employed therapeutically at the present time was isolated in 1901 by Piorkowski from two turtles which had succumbed to tuberculosis. After fifteen years of cultivation on artificial nutrient media and repeated passages through turtles, a strain of tubercle bacillus was obtained which is nonvirulent and nontoxic to man. Since experiments on animals showed also that this turtle tubercle bacillus produced a noteworthy immunizing effect, it is now possible to prepare the long desired vaccine from living tubercle bacilli which can be applied to human beings without danger of infection. It has been found most suitable to employ a mixture of bacilli cultivated at 98.6° F. and those cultivated at 68° F. It is not claimed that the vaccine restores organs which have undergone irreparable pathological changes, but is only applicable in the early stages of the disease. Just as in vaccination against smallpox, it is assumed that complete immunization against tuberculosis is established by a single injection of Piorkowski's vaccine.—*Active Immunization by Means of Nonvirulent and Nontoxic Living Tubercle Bacilli, C. D. Aaron, N. York M. J., January 15, 1921, cxiii, 91.*

Classification of Tuberculosis.—A new and definite method of classifying cases of tuberculosis should be adopted, and its use made obligatory for all medical officers of dispensaries, hospitals and sanatoriums dealing with County Council or State patients. The classification put forward is not designed to group cases according to their suitability for any particular individual treatment, but to separate cases into definite categories, in order to systematize their observation and disposal, and to form standards by which the results of treatment can be compared. It is based on the presence or absence of tubercle bacilli in the sputum and the presence, absence and extent of moist sounds (crepitations). Experience and statistics go far to prove that in the main the prognosis is distinctly worse in those with positive sputum and with definite moist sounds in the lungs. The following classification of suspected and diagnosed cases of active tuberculosis is suggested: A: Stage of observation of suspected active pulmonary tuberculosis in adults and children. 1. Patients exhibiting signs and symptoms suggestive of pulmonary tuberculosis with indefinite physical signs in the chest: require dispensary observation. 2. Patients after one month's dispensary observation in whom the signs and symptoms suggestive of pulmonary tuberculosis persist and the physical signs in the chest remain indefinite: if undiagnosable, require observation in hospital. B: Diagnosed cases of active pulmonary tuberculosis in adults and children over twelve years. B1: Early cases: (a) Tubercle bacilli absent. Physical signs in the chest indefinite or limited to the physical signs of fibrosis. Diagnosed after observation in dispensary or hospital. (b) Tubercle bacilli positive. Physical signs in the chest indefinite or limited to the physical signs of fibrosis. B2: Medium cases: (a) Tubercle bacilli absent. Definite moist sounds (crepitations) limited to one apex. (b) Tubercle bacilli present. Definite moist sounds (crepitations) limited to one apex. B3: Advanced cases: (a) Cases with crepitations extending lower than the apex on one side or present on both sides. (b) B1 and B2 cases plus tuberculous laryngitis. (c) Acute or miliary cases. B4: Fibroid phthisis, tuberculous. B5: Cases of bronchitis, emphysema or asthma plus pulmonary tuberculosis. C: Pulmonary tuberculosis in children under twelve years. D: Surgical tuberculosis: (1) Children under twelve years. (2) Adults and children over twelve years. E: Stage of arrested tuberculosis.—*Suggested Classification of Tuberculosis, W. B. Knobel, Tubercle, December, 1920, ii, 110.*

Fight Against Tuberculosis in Large Communities.—This report is based on a report by F. M. K. Menzies on tuberculosis in London. In London, which is particularly threatened by phthisis, although its tuberculosis mortality is one of the lowest in Europe, an educative and prophylactic organization which is relatively very extensive reaches out of 80,000 patients only half of the new cases occurring in a year. Only about a quarter of the latter are protected sufficiently early; the others are taken in hand too late, at a time when vital resistance is nearly exhausted, and, as a matter of fact they die within a few years. The treatment of cases which are bound, anyway, to sink lower and lower is overemphasized, and as a result the organization against tuberculosis supervises, educates and protects only a trifling portion of the 200.000 human beings who are daily subjected to massive infective doses. In order to be free from the technical errors of partial organization, a complete prophylactic scheme requires an increase of present resources. The defects in the campaign against tuberculosis are only partially due to economic and social difficulties. General prohylactic measures begin with the fight against the bovine bacillus. Milk analysis shows the presence of Koch's bacillus in 6 per cent out of 943 samples collected for bacteriological examinations. A veterinary inspection of the suspected herd and the slaughter of the diseased animals are necessary. Compulsory notification of cases of tuberculosis yields often unsatisfactory results. In one Metropolitan borough out of 305 deaths attributed to tuberculosis in 1915, 31 per cent were only reported at death, 19 per cent were reported within a month of death, 16 per cent were within six months. Dispensary hours are too short and too crowded. The waiting period for institutional treatment is too long, namely from seven to fifteen days for an ex-soldier, twenty-eight days on the average for an adult, and eight to twelve weeks for a child.—*Organization of the Fight Against Tuberculosis in Large Communities, F. Humbert, Internat. J. Pub. Health, November, 1920, i, 371.*

Health Letters.—The health letters presented in this monograph represent the most consistent effort at health education in the community. They are reprinted from the Framingham *Evening News*, in which paper they have been carried every Saturday night for the last three years. There is presented, first, a special series on tuberculosis, which is followed by representative collections of health letters on various health topics. The letters have geen prepared by several members of the Health Demonstration staff. The special series on the fight against tuberculosis comprises letters on how we can fight tuberculous infection, on public, personal, home and food hygiene, the reduction of deaths from tuberculosis, etc. The selected groups of letters on general health topics comprise letters on tuberculosis in childhood, on the cured tuberculous, on regular medical examinations, child hygiene, safe milk for the children, the children's health camp, overwork, summer hygiene, dental care, self-doctoring, the need of rest and vacations, community hygiene and the dangers of breaking quarantine, flies, filth, and fever. The letters about special diseases give general information about the common cold and its prevention, influenza, heart disease in children, typhoid and scarlet fever, smallpox and vaccination, measles and malaria. Poison ivy, oak and sumac, mental hygiene and social diseases, and war work campaign are dealt with.—*Health Letters* (*Reprinted from the Framingham Evening News*), *D. B. Armstrong, December, 1920.*

The Film for Tuberculosis Propaganda.—The film which is being worked out by the central committee for the fight against tuberculosis will contain valuable information about the tubercle bacillus, differential diagnosis and therapeutic measures, various internal and external manifestations, and the social question and prophylactic measures. Clubs and professional organizations will be the sponsors of such productions. Moving picture theatres, available in the early afternoon and Sunday mornings, offer all technical requirements. An accompanying explanatory lecture by a physician will make the public performances interesting. But all these measures reach only a small proportion of the population and mostly those who need them least. In order to be effective they must reach all. This is only possible by education in the schools before graduation. There is no more convenient and effective measure than the film. Educational films on hygiene should be incorporaged in the curriculum of the schools.—*Der Film im Dienste der Tuberkulosebekämpfung, C. Thomalla, Tuberculosis, October, 1920, 257.*

Tuberculosis Problems in State Hospital Practice.—The general problems of tuberculosis and prevention in state hospital practice are more difficult to handle than in private life. The wards are overcrowded by lack of sufficient buildings, and the nursing force is inadequate. With the normal patient, the early symptoms of tuberculosis arouse his alarm and tend to bring him under treatment. With the mental cases, it is unusual to obtain any help of a subjective nature. Coughing among the tuberculous insane is lessened and often absent. Coöperation during physical examination is poor, making early diagnosis difficult. It has been surprising how few pulmonary hemorrhages have occurred. With a death toll of 315, only 5 suffered from hemorrhage. The treatment in general is similar to the usual sanatorium practice. Rest, fresh air, sunlight and forced feeding are at once started. No patient is allowed up who shows an afternoon temperature of 100° or over. For routine medical therapy the syrup of hypophosphites with creosote and, formerly, liberal but judicious use of whiskey and sherry for its tonic and fuel value have been used. The incidence of tuberculosis may occur in any form of insanity, other than dementia precox.—*Résumé of Tuberculosis Problems in State Hospital Practice, D. D. Durgin, Long Island M. J., November, 1920, xiv, 433.*

Controlling Tuberculosis.—The control of tuberculosis by means of community machinery or community activity should work along four lines: prevention of infection, discovery of the cases, treatment, and building up of resistance. Infection is prevented by the educational machinery, by visiting nurses and by the hospitals for advanced cases. To discover the cases, the clinic or dispensary, the nurse, the medical consultant and the medical examination drive on the sickness survey have proved very valuable. The care and treatment of the sick are carried out by the sanatorium, the nurse, the dispensary, relief agencies and the vocational work shop. The fourth group which is not so well defined, includes the open air school and fresh air class, both for subnormal and normal children, the fresh air camp, and summer schools.—*Controlling Tuberculosis, P. P. Jacobs, Long Island M. J., November, 1920, xiv, 430.*

Educational Training in Tuberculosis.—In the treatment of tuberculosis, perhaps more than in any other disease, failure and disappointment, while discouraging, have not daunted workers. There are waves of advocacy of this or that method of treatment, which in turn are condemned with often unnecessary emphasis. Yet in almost all methods of treatment there are elements of good, depending on the individual case. One reason for such diverging views is found in the impossibility of the tuberculosis worker obtaining adequate experience in the employment of all methods, or in his inability to apply them at that particular phase of the disease when they would afford the greatest prospect of success. The reason for this is an absence of team work, and the swamping of therapeutic effort by administrative details. The failures in the tuberculosis campaign are not entirely due to defects from without; they may, at any rate, in part be ascribed to errors from within. And yet such defects are ignored, our diagnosis as to cause of failure is faulty, our resultant treatment for that failure is correspondingly incorrect. The present tendency appears to be to spend money lavishly on tuberculosis schemes, but to do little to ensure that their conduct is entrusted to highly skilled workers. The evil commences in our medical schools. The medical student of today is the medical practitioner of to-morrow, and the general practitioner is our first line of offence against tuberculous disease. Comparatively little interest is taken in the instruction in the prevention, diagnosis, and treatment of the disease in the medical schools. There is not a single professor of tuberculosis in any teaching school in England or Ireland, and only two, both recently appointed in the United Kingdom. Few, if any, medical students ever enter any of the special institutions for tuberculosis, except as patients. The student would derive immense advantage if opportunities were afforded him for such instruction. The teacher also learns much in teaching. His work must be of a sufficiently high order to meet the needs of his pupil, who is quick to scorn incompetence, but equally impressed by knowledge and efficiency. A proper teaching unit should afford the fullest facilities for theoretical and practical instruction in all aspects of the tuberculosis problem. And these facilities should be available not only for the student, but also for the practitioner of medicine. The community would benefit even more than the practitioner, and if the latter is prepared to give up his valuable time the former should at least see that he does so without expense to himself. If it pays the state to educate without fee an elementary school student, how much more profitable must it be to train further a valuable public servant.—*Training in Tuberculosis, H, Gauvain, Brit. J. Tuberc., January, 1921, xv, 1.*

Coöperative Tuberculosis Campaign—Suggestions: 1. In view of the fact that there are more herds under supervision than can be promptly taken care of by regularly employed agents of the Bureau, and owing to the increase in applications from owners for herd tests under the accredited plan, much of the work now being done by Federal and State agents could be carried on by practising veterinarians, which would speed up the work, and in the future more recognition should be given the practising veterinarians. 2. There should be a more uniform interpretation of the accredited plan throughout the United States. 3. Steps ought to be taken to bring about a more uniform method for applying and interpreting the various tuberculin tests. 4. In so far as is practicable, the form of contract or agreement between the owner and Bureaus should be made more uniform. 5. Provision is to be made in the accredited plan whereby future amendments to the plan will automatically apply to existing contracts, thus doing away with the necessity of entering into new agreements or contracts with owners whose herds are already under supervision. 6. More attention must be given to preventive measures. 7. Full value up to a prescribed amount is to be paid for both native and interstate reactors which on autopsy show no visible lesions. 8. The practice of slaughtering all reactors is robbing the country of many of our choicest animals, which should be preserved to perpetuate valuable blood lines, and a greater united effort should be made to estabish more Bang herds on separate farms for keeping such animals. 9. The accredited plan must be amended in a few minor details.—*The Co-operative Tuberculosis Campaign in Pennsylvania, T. E. Munce, J. Am. Vet. M. Ass., March, 1921, lviii, 706.*

Dispensary, Sanatorium and the Tuberculosis Officer.—At the dispensaries, attempts may be made to sort out so called early cases, but very few come under the observation of the tuberculosis officer, and so many middle cases are in such urgent need of treatment that sanatoria receive very few early cases. The various public and municipal sanatoria are practically monopolized by middle and advanced cases. One reason for the want of understanding and lack of action is that tuberculosis officers are compelled to treat what they cannot find. During their medical course they have not been taught to seek or recognize the really early signs and symtoms of tubercuosis. All effort will prove fruitless until treatment and prevention advance together. The tuberculous must learn to live the life of consumptives and they must be provided with permanent work. They must be capable of earning as much as possible to this end. Medicine, sociology, economics and psychology are involved in the tuberculosis question. The dispensary medical officer is discouraged and hampered on all sides. The system is wrong and except in rare and notable instances a complete failure. The head of the tuberculosis department should not be hampered by too varied duties or enmeshed in red tape and he should possess more knowledge. He should have time and facilities to study experiments, observations or publications bearing on his own work. He should possess the working knowledge of the extent to which treatment of patients in their own homes is beneficial, how far work can be arranged for, either in a borough or county area, the economics of the problem, the home conditions of the people and the relation of these to questions of infection, workshop and factory conditions, hours of toil and industrial fatigue. It would benefit the patient and community greatly if the tuberculosis officer were encouraged to deal with a case thoroughly. The dispensary officer and the sanatorium physician are kept in their little compartment and there is no expert head. *The Dispensary, The Sanatorium and The Tuberculosis Officer, The Weak Links in a Chain, P. C. Varrier-Jones and G. S. Woodhead, Lancet, January 29, 1921, cc, 256.*

Statistics on Infant and Tuberculosis Mortality during the Eighteenth Century: The First Census in Vienna.—The indefinite terminology of the times makes it difficult to give exact figures. The tuberculosis mortality figures in Vienna for the years 1752 and 1753 given in percentage of the total mortality and various age periods were

	per cent
1 to 4 years	27.4
5 to 9 years	36.0
10 to 14 years	31.4
15 to 19 years	28.0
20 to 39 years	25.9
40 to 49 years	26.4
50 years and over	20.8

In the classes from fifteen to thirty years, 50 per cent of the deaths were due to pulmonary tuberculosis.

Mortality figures per 1000 inhabitants at different periods

YEARS	TOTAL	TUBERCULOSIS
1752–1754	36.2	5.3
1867–1870	32.9	8.6
1871–1880	32.9	7.8
1881–1890	27.5	6.9
1891–1900	22.6	5.0
1911–1914	16.1	3.2

Tuberculosis mortality according to age per 1000 inhabitants

AGE	VIENNA 1752–1754				VIENNA 1910–1911	PARIS 1901–1905
	Male	Female	Total			
1–4	10.67	9.40	23.3	10.0	4.4	5.2
5–9			7.5		1.6	1.9
10–14			2.5		1.0	1.2
15–19	2.03	0.90	1.35		2.3	3.0
20–39	2.71	1.65	2.13		3.3	4.2–6.1
40–49	5.34	2.71	3.93		4.0	6.5
50*	11.13	8.63	9.83		4.0	6.0–2.9

* And over.

Those periods having a high total mortality also had a high tuberculosis mortality (up to fourteen years and over fifty years). The 1752 and 1753 statistics differ from those of the twentieth century in that the incidence is higher in the lower ages and after the twentieth year as compared to the periods of puberty. Seemingly tuberculosis during this period was more active in the younger years and thus exhausted itself, resulting in a lowered mortality during the periods of puberty and middle age. It is possible that the living conditions of the modern manufacturing city may be a factor in accounting for the higher mortality during the middle age period. In 1753 there were 452 Jews in Vienna. The mortality from 1748 to 1755 was 69 or 18.9 per 1000 (19.3 male, 17.3 female) while the mortality for all of Vienna was 33 per 1000. In 1752–3 the mortality among the Jews of Vienna was 31 per 1000. The Jews had a low infant and childhood mortality while at puberty it equalled the general mortality. The Jewish tuberculosis mortality was 10 to 12 per 100 deaths while the total in Vienna was 25 per 100 deaths, or a tuberculosis mortality of 19.2 as compared to 52.7 per 10,000 inhabitants. Jewish children between the ages of 0 to 14 years had a tuberculosis mortality of 2.1 to 2.8 per cent while Vienna had 10.1 per cent.—*Zur Kenntnis der städtischen Mortalität im 18. Jahrhundert mit besonderer Berücksichtigung der Säuglings und Tuberkulosesterblichkeit* (*Wien zur Zeit der ersten Volkszählung.*), *S. Peller, Ztschr. f. Hyg. u. Infektions-krankh., 1920, xix, 227.*

Tuberculosis in Canada.—The estimated annual number of deaths from tuberculosis in Canada now amounts to 9,096. In the Dominion census for 1901 the deaths were estimated at 9,709, a decrease during the past two decades of over 30 per cent. This decrease is due to three factors: (1) the lessened infection in the homes from which tuberculous patients have been removed to hospitals and sanatoriums; (2) the earlier recognition and the earlier and better treatment of patients both in their homes and in sanatoriums; and (3) the better home and living conditions, especially in regard to ventilation, sanitation and personal hygiene. While there is this decline, there have been, and still are, more deaths from tuberculosis than are reported. The Canadian Association for the Prevention of Tuberculosis and the numerous local associations throughout the dominion have done a large amount of educational work during the past twenty years, and as a result dispensaries, preventoriums, sanatoriums, hospitals and laboratories have been provided in various centers. Much legislation, such as notification, antispitting laws and disinfection has been passed. The federal government supports this association which works in coöperation with both the federal department of health and the various provincial health authorities, all of whom are represented on its executive.—*Tuberculosis Problem in Canada, G. D. Porter, Publ. Health J., January, 1921, xi, 1.*

Cleveland Health Survey.—Cleveland is admirably equipped with legislation for the prevention of the spread of the great white plague. The inspection of milk is fairly well enforced and much is done in providing milk at cost for tuberculous citizens. The enforcement of housing ordinances, however, is wofully inadequate. Overcrowding is most dangerous and must be stopped in order to stamp out tuberculosis. The proper legislation for the segregation of advanced tuberculosis is rarely employed. Little attention is paid to the antispitting ordinance. No arrests had been made for this violation from January, 1919, to June, 1920. The Warrensville Tuberculosis Sanatorium is a model institution. Four to five doctors are on the staff, and 254 beds devoted to advanced cases. Other institutions for pulmonary cases are the Ohio State Sanatorium, with 23 beds reserved for Cleveland patients; the city hospital, with 100 beds, the State Insane Hospital with 6 beds for Cleveland; and the general hospitals which care for 10 to 12 cases. The antituberculosis league is somewhat at a standstill, after years of good work. The work of this league should and must be extended to meet the need in Cleveland. The Associated Charities (one of the best organizations of this kind in the country) and the Red Cross are doing much good. Little enthusiasm is shown by Cleveland physicians, owing, no doubt, to the lack of opportunity for special study in this field. It is hoped that the Western Reserve Medical School will supply a postgraduate training course in tuberculosis, open to all doctors, and that a consultation service, with the coöperation of the Western Reserve University may be established. The factory authorities should do more in detecting tuberculosis in its incipiency. Over half the cases found are advanced ones, with little hope for a cure. Annual or semiannual examinations of all employees is recommended. There is only one nurse for every six thousand inhabitants. There should be twice that number. There must be at least 500 more beds in Warrensville, the city and general hospitals devoted to the care of tuberculosis patients. An active educational campaign is needed.—*A Popular Summary of the Cleveland Hospital and Health Survey, 1920, 13.*

Tuberculosis of the Lip.—The case here reported represents an unusual instance of solid tuberculoma of the lower lip with ulcerations of the buccal mucosa associated with a chronic pulmonary tuberculosis of the fibroid type. Tuberculosis of the lip must be differentiated from chancre and epithelioma. A positive diagnosis rests on the finding of tubercle bacilli and the characteristic histology.—*Tuberculosis of the Lip, E. P. Zeisler, Arch. Dermatol. & Syphilol., January, 1921, iii, 14.*

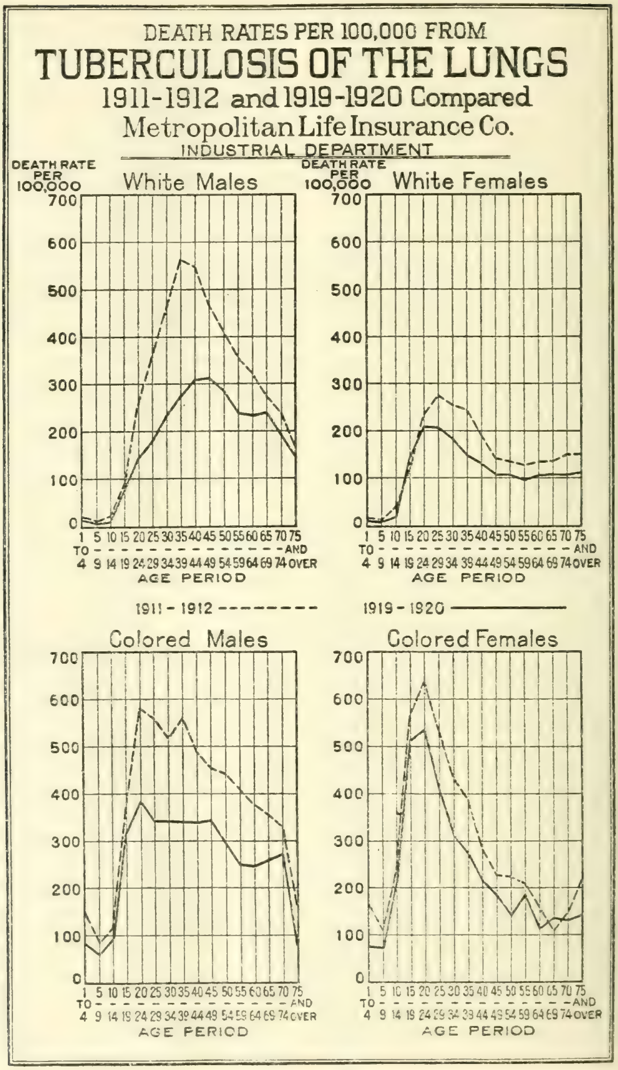
Pulmonary Tuberculosis in the Senegalese.—The Senegal negroes showed a type of tuberculosis common in children of middle Europe. The resistance however was somewhat increased. An aerogenous infection showed involvement in the lungs and also in the tributary lymph channels and nodes, progesssing to an exudative and caseous and miliary process. The type of disease is probably due to the unobstructed lymph channels of the lungs.—*Bemerkungen über Phthise bei Senegalnegern, G. B. Gruber, Ztschr. f. Tuberk., October, 1920, xxxiii, 23.*

The Conquest of Tuberculosis.—The attack upon tuberculosis seems to be succeeding to a degree not dreamed of by advocates of the work ten years ago. The health statistics of wage-earners insured in the Metropolitan Life Insurance Company record remarkable declines in the prevalence of tuberculosis. These reductions, moreover, are greatest at those age-divisions of life where the tuberculosis death rate is highest, where it creates the heaviest social damage in terms of broken and dependent families, and where it removes wage-earners from industrial life at a time when productive effort counts for most. Such gains deserve detailed consideration and will give further impetus to this fruitful work. The pulmonary tuberculosis death rate for insured white males between twenty-five and forty years of age in the two years 1919 and 1920 combined, was one-half of that for the combined years 1911 and 1912. At these age-divisions ten years ago, pulmonary tuberculosis prevailed at a rate of 4 to 6 deaths per 1000 persons annually; during the past two years, the tuberculosis death rate of this age-division of life varied from 2 to 3 deaths per 1000 persons exposed to risk. And this is not all of the good news. Beyond age forty and up to sixty-five years of age, there were reductions in the pulmonary tuberculosis death rate of white males varying from 44 per cent at the period forty to forty-four years, to 27.5 per cent at the age group sixty to sixty-four years. Beyond age sixty-five, the decline in the pulmonary tuberculosis death rate in this group was not less than 12 per cent. At the age group twenty to twenty-four years, when the stresses of industrial life first begin to show their effects upon the tuberculosis death rate, there was a decline of 45 per cent in the death rate. Among adolescents of the ages fifteen to nineteen years, the reduction was 27 per cent. A substantial reduction was observed also among white male children under ten years of age. The facts for insured white females and for colored males and females tell practically the same story of success in the control of the factors causing death from pulmonary tuberculosis. For these groups, also, the greatest relative declines in the tuberculosis death rate occurred in the main working period of life. For the age-period thirty to thirty-four years, there was a reduction of 47 per cent among white females. It is worthy of special comment that the savings in tuberculosis among this latter group were relatively less than among insured white males at all ages between five and sixty-five years, but after this age the savings were twice as great as among insured white males One of the anomalies of these recent figures is that there was an increase of about 3 per cent in the pulmonary tuberculosis death rate of white females in the ages between fifteen and nineteen years. There were greater declines in pulmonary tuberculosis mortality among negro children under fifteen years of age than among insured white children. But it should be remembered that even in the most recent years the death rates for colored children are still from six to ten times as high as among white boys and girls. Beyond age fifty, colored males show a greater decline in the death rate than do insured white males. The following table gives the percentage reductions in the pulmonary tuberculosis death rate.

Tuberculosis of the Lungs.—Percentage reduction, 1919–1920 from 1911–1912 death rates Metropolitan Life Insurance Company —Industrial Department.

AGE PERIODS	WHITE		COLORED	
	Males	Females	Males	Females
All ages — 1 and over....	42.4	22.2	30.7	21.3
1 to 4......	14.4	22.2	40.8	55.0
5 to 9......	29.5	10.8	32.1	28.5
10 to 14......	7.4	6.3	11.0	11.9
15 to 19......	26.5	3.4*	19.7	9.0
20 to 24......	45.0	11.8	33.1	15.9
25 to 29......	49.5	24.9	38.7	22.0
30 to 34......	49.5	46.6	33.6	27.2
35 to 39......	50.9	37.9	39.1	29.3
40 to 44......	43.7	32.1	31.2	25.5
45 to 49......	33.8	28.0	24.7	19.5
50 to 54......	30.1	23.8	32.4	36.7
55 to 59......	32.8	22.0	38.2	10.2
60 to 64......	27.5	24.8	35.0	30.0
65 to 69......	11.7	24.3	24.6	31.9*
70 to 74......	18.4	32.6	17.2	11.0
75 and over...	12.0	30.8	49.4	35.0

* Percentage increase.



DEATH RATES PER 100,000 FROM
TUBERCULOSIS OF THE LUNGS
1911-1912 and 1919-1920 Compared
Metropolitan Life Insurance Co.
INDUSTRIAL DEPARTMENT

We may conclude broadly from these data that it has been possible for all of the community forces working together so to modify the environmental and perhaps also the hereditary factors in tuberculosis as to reduce very materially the number of lives formerly lost to society on account of this disease. At those age-ranges where environmental factors are not so important and where, perhaps, the constitutional element is uppermost (among children and the aged), the death rate has not declined so rapidly. The chart shows the changes which have occurred in the eight years—*From Statistical Bulletin; Metropolitan Life Insurance Co., March, 1921, ii, 1.*

Heredity in Tuberculosis.—H. M. King of Liberty, N. Y., observed in 242 cases of tuberculosis that the percentage of individuals with a tuberculous parentage was smaller than that of those with a nontuberculous parentage, and that the children of tuberculous parents when attacked by disease showed a greater resistance and a stronger tendency to recover than other persons. The observation of Adams is that children of tuberculous parents are certainly more exposed to infection, but that it seems possible that they are more resistant to the disease than other children, and that this fact may to some extent account for the diminishing mortality from tuberculosis. In the study of 1000 cases it was found that over 60 per cent of the cases treated gave no family history. The results of treatment were compared under identical conditions of the two classes of patients. In each group the percentage of patients who failed to respond to treatment was less among those with a family history than among those without. The gravity of the history made little difference. There was marked difference in the greatly improved group where the results also are in favor of those with a family history. The question is raised whether it is not probable that the decrease in the death rates from tuberculosis is largely due to an acquired or hereditary immunity which is steadily raising the resistance to the onset and course of the disease, and that the cases of tuberculous families are only examples of massive infection during infancy and childhood in which the resistance is overcome.—*Heredity in Tuberculosis, A. Adams, Tubercle, January, 1921, ii, 145.*

What the War has Taught with Regard to Predisposition to Tuberculosis.—The fact that very many soldiers harbored the tubercle bacillus within their bodies, and that only a certain number of these developed tuberculosis, proves how the disease singles out for its victims those with lowered organic resistance which is accentuated by a wartime environment. The tubercle bacillus in itself is not sufficient to produce the disease: the individual must also have a hereditary predisposition. Viewed from this standpoint, the danger of contagion must always be subordinated to the predisposing factor. This determinism plays a greater part in tuberculosis than in any other infectious disease. It is only the soldier who has a constitutional predisposition that develops tuberculosis under the stress of war.—*La predisposizione alla tubercolosi e gli insegnamenti della guerra, F. Vincenzo, Tubercolosi, July, 1920, xii, 201.*

Industrial Tuberculosis and the Factory Dust Problem.—Any useful method of dust determination must include particles ranging down to one micron in diameter. Methods of estimation of atmospheric dust may err by revealing only the very large particles present in the air or by including particles too small to be of any sanitary significance. The desideratum is a method which will reveal the number of dust particles of a diameter between 10 microns and 1 micron. Of the 3 methods which are in use at the present time and which appear to meet these requirements the Palmer apparatus appears to be the most satisfactory. In this method the air to be sampled is drawn through water in a shallow trap at such a rate as to break up the water into a fine shower of spray in a glass bulb above, and this spray retains the dust in the air and finally washes it down into the trap. After the completion of a run, the dust which has accumulated in the water may be estimated by direct microscopic enumeration of the number of particles in a Sedgwick-Rafter cell and by weighing the dust after filtration through a Gooch crucible. The Palmer water spray apparatus is fairly convenient and portable. It yields only about 60 per cent of the total dust present in the air. The average dust content of pure outdoor country air was 7100 to 50,300 dust particles per cubic foot. Of three samples collected outside the Woolworth building, one from the street level showed 118,000 particles per cubic foot, one from a window on the tenth floor, 72,000, and one from a window on the fifty-eighth floor, 23,000. The average dust content of the air in various types of industrial establishments was studied. It ranged from values between 100,000 and 200,000 dust particles per cubic foot in factories where the dust problem is well cared for to figures 100 or even 1000 times as great in the worst types of grinding shops and abrasive factories. There are, in general, four different methods of protecting the worker against the influences of industrial dusts, which may be classified as follows: the substitution of wet processes for dry processes; the conduct of dust producing operations in enclosed chambers; the removal of dust by hoods equipped with exhaust draft; and the use of respirators and helmets. The use of moisture may or may not be effective, depending on the details of the process and the method by which the water is applied. The way to determine the efficacy of any method is by a study of the actual dust content of the air. The method of controlling the dust hazard which consists in the carrying out of dust producing processes, such as sifting, crushing, tumbling, and the like, by mechanical devices in enclosed chambers, has proved notably successful in dealing with poisonous dusts. Excellent results may be obtained from the use of hoods equipped with a system of exhaust ventilation sufficiently powerful to remove the dust as it is produced and to carry it away from the workroom, in certain types of grinding and polishing, which cannot be carried on by wet methods or in enclosed chambers. Defects in construction of the hood system are common. In certain industrial processes, as in packing operations, in marble and granite working, and in the sand blasting of large castings, it is impossible to keep the air of the work place free from dangerous concentrations of mineral and metallic or poisonous dusts by any of the methods mentioned. In such cases the only alternative is the wearing of respirators which filter out the dust particles from the air before it is drawn into the respiratory tract, or of helmets which exclude the dusty atmosphere more or less completely from the mouth and nose and supply pure air for breathing from some other source. All such devices are uncomfortable and irksome to the wearer and should be avoided wherever possible. From the standpoint of the actual dust content of the air which would be respired by a sand blaster, the use of the respirator alone evidently fails to provide an adequate protection. From the standpoint of per cent removal, on the other hand, the respirator showed a high efficiency which should make it a fairly satisfactory protective device for use in a work place where the initial dust content is not enormously high. The use of the helmet and respirator in combination produced a reduction from an average of 58,330,000 dust particles per cubic foot of air to an average of 2,355,000, a reduction of 96 per cent. These results are distinctly better than those obtained with the respirator alone, but the air was still too dusty to be respired with safety. The tests with positive air pressure showed that the dust content of the air collected in this way, with an average air supply of 2.9 cubic feet per minute to the interior of the helmet, ranged from 18,000 to 329,000 one-fourth standard unit particles and average only 151,000 such particles per cubic foot. It is important that standards of a reasonably definite nature should be established by which the adequacy of protective devices can be judged in any given case. Only three efforts have so far been made to set definite standards of this kind for industrial dusts. They were made by the Miners' Phthisis Prevention Committee of South Africa, by Higgins, Lanza, Laney, and Rice in a study of the mines in the Joplin district, Missouri, and by the authors. The latter suggest that a fair measure would be obtained by specifying that the suction head in the exhaust pipes of a polishing shop should at no point fall below 2 inches, and should average 3 inches. The velocity of the exhaust air current maintained at the throat of the exhaust duct should not fall below 1500 feet. It is tentatively concluded that in a polishing shop the weight of dust in the air can be constantly kept below 0.06 mgm. per cubic foot and should not average over 0.03 mgm., while for a grinding shop these values should perhaps be doubled. The dust content of the air can be kept generally under 300,000 one-fourth standard unit particles per cubic foot and should not average over 200,000 such particles. These standards are subject to revision with the development of a wider knowledge of the air conditions in representative workrooms.—*Industrial Tuberculosis and the Control of the Factory Dust Problem, Part II, C.-E. A. Winslow, and L. Greenburg, J. Indust., Hyg., February, 1921, ii, 378.*

Infectivity of Tuberculosis.—The writer takes the view that the great majority of the mates of tuberculous husbands or wives sooner or later show signs or develop symptoms of tuberculosis; and further believes that the great majority of those infected recover, and make a speedier recovery, than most tuberculous patients. If a man or woman of a tuberculous type marries, they usually do not marry another of the same type. No one can deny that the individual resistance to tuberculosis varies within wide limits, or, indeed, that there may be varieties of low resistance, but the main factor in spreading the disease that suggests itself when visiting the homes of tuberculous patients is infection. The question of direct infection apart from conjugal cases is more difficult, and would be almost hopeless to attack in any but rural districts. The writer has sometimes found a little colony of tuberculous persons in a more or less isolated spot, such as one street of a village, and is inclined to attribute the existence of such a colony to conditions of infection due to carelessness, rather than to the influence of the local climate, or the prevalence of some special wind. These considerations seem to indicate that the attempt to check tuberculosis should be made by treating it as an infectious disease, dealing first with obvious sources of infection in the home and the factory. These measures would entail no great hardship to individuals or any dislocation of society, and we might very well find after their adoption that the infection was becoming less universal, and further means to prevent the disease completely would suggest themselves.—*The Infectivity of Tuberculosis, E. Ward, Brit. J. Tuberc., January, 1921, xv. 5.*

Lung Wounds and Pulmonary Tuberculosis.—In addition to previously reported cases (*Ztschr. f. Tuberk., xxvi, no. 1, and xxix, no. 1*) 18 new ones are reviewed. These are divided into those with old inactive tuberculosis which was not reactivated by the lung wound, and those which developed active disease following lung wounds. In the first group there were 3 cases. The wounds were produced by shrapnel, grenades, and rifle. Definite evidence of active tuberculosis did not exist and the X-ray showed in 2 cases very slight changes at the hilum, and by physical examination a slight impairment of note over the apex. In group two there were 15 cases, in 2 of which there was a previous tuberculosis. In 3 of the remaining 13, X-rays were not taken. In 4, plates showed no evidence of a previous tuberculous process, in 2, questionable and 6 definite. The wounds were produced by rifle bullets in 6, hand grenades in 5, shrapnel in 3, and unknown in 2. In summarizing one finds that of over 6000 patients who during the world war were taken into the sanatorium at Beelitz only 75 had lung wounds. Eight additional patients came after discharge from the army. Among the total of the 83 patients no tuberculosis could be demonstrated in 37, or inactive old tuberculosis foci were not activated, and in 46 active disease became manifest and was most likely the result of the lung wound. Conclusions: A latent tuberculosis may be activated by lung wound but this is an infrequent occurrence.—*Lungenschüsse und Lungentuberkulose: eine letzte Beobachtungsreihe und Schlussbetrachtungen, G. Frischbier, Ztschr. f. Tuberk., October, 1920, xxxiii, 7.*

Chest Wounds and Pulmonary Tuberculosis.—Among 2359 army men in the sanatorium at Überruh there were 33 who had chest wounds. Records of 10 of the 33 cases were very incomplete. Of the remaining 23, 14 had perforating lung wounds, in 1 case both lungs; 3 had penetrating lung wounds; 6 had chest wounds with questionable injury to the lungs; 1 had a shoulder wound. The wounds were caused by rifle bullets in 7, by grenades in 6, by machine propelled bombs or grenades in 5 instances, and in 2 the cause was not recognized. Open tuberculosis occurred in 9 cases, closed in 14. Among the latter were 12 active cases and two probably active, so that there were 21 cases of known active tuberculosis. In 9 cases there was no family history of tuberculosis nor a history of previous tuberculosis. Of these 4 were open cases and 5 active closed cases. The remaining 7 cases who had no family history or previous history of tuberculosis showed old tuberculosis, reactivated after shorter or longer periods after the wound. The time elapsing between wounding and symptoms of tuberculosis ranged from one month to five years. The wounded lung was first and more severely involved in 17 cases. In 5 additional cases the more severely wounded lung was not the more seriously diseased. Summary: 1. Reactivation of old tuberculous foci in the lung, through wounding, appears to be not so infrequent as is commonly believed, and, although trauma is of prime importance in the most cases, nevertheless physical and mental strain as is encountered in the field, as also insufficient nourishment, play a very important rôle. 2. The prognosis of such cases as developed pleural thickening and adhesions must be guarded. 3. Two cases were observed that were apparently perfectly well, in which there was no family history of tuberculosis and in which no tuberculosis could be demonstrated by physical and X-ray examination before wounding, and in these most likely there was a new infection. 4. A close relation between the trauma and location of the tuberculous lesion existed in the sense that the wounded lung was the first to show the disease and the more severe disease in the majority of cases. 5. The period between wounding and the appearance of active tuberculosis was shorter in those cases which had received previous treatment for tuberculosis than in those in which no previous family history or previous tuberculosis could be substantiated.—*Brustschüsse und Lungentuberkulose, O. Seiter, Ztschr. f. Tuberk., October, 1920, xxxiii, 1.*

Tuberculosis and Reinfection.—In 1908 Calmette addressed a letter to practising physicians in France on the subject of Marfan's "law," which emphasizes the rarity of progressive tuberculosis in adults who in infancy have had and been cured of tuberculous adenitis. The answers received confirmed the law. In his recent work, *L'Infection Bacillaire et la Tuberculose,* Calmette relates many experiences of different workers on the Koch phenomenon, concluding that the consumptive is one who has received since childhood successive more or less massive reinfections. Bushnell in his recent *Study in the Epidemiology of Tuberculosis* is emphatic in stating that reinfection cannot occur after a primary infection has been established, supporting his contention with the facts on the absence of reinfection in other chronic diseases as syphilis and malaria. Against Bushnell's statement that the subject may die of extension of the disease, but in pulmonary tuberculosis will preserve to the end of his life the first degree of immunity and develop no distant foci due to his own bacilli, stands the frequency of ischiorectal abscesses and laryngeal lesions, which are not terminal. Theobald Smith holds the view that a bacillus coming to the lungs from without has as good a chance as one carried there from a preëxisting focus. The size of the reinfecting dose is the vital factor. Tuberculization of the race is for the most part beneficial, and humanity may be to a considerable degree protected by the primary infection. However it does not as yet seem possible to be absolutely certain that reinfection from without does not occur.—*Tuberculosis and Reinfection, Editorial, J. Lab. & Clin. Med., December, 1920, vi, 162.*

The Disinfecting Power of the Solar Rays upon Tubercle Bacilli.—Preparations of tubercle bacilli in pure culture, pus from tuberculous glands and fresh expectoration were made in the thinnest possible layers and then after varying exposures to sunlight were dissolved in physiological saline solution for inoculation into animals. For controls, preparations dried in the air were likewise inoculated into guinea pigs. Special filters variously constructed with uviol glass containing copper sulphate solution were employed to isolate the ultraviolet rays. The exposures were made in Leysin at a height of 1360 meters only on very sunny days between the hours of 10 a.m. and 2 p.m. when the maximum intensity of light was found. During the exposure, solar intensity, temperature and relative humidity were determined. The conclusions reached were the following: 1. The disinfecting power of sunlight against virulent tubercle bacilli at an altitude of 1360 meters under the most favorable conditions, in the summer months of June to August, was revealed in about a half hour, in the fall and spring in about an hour and in the winter months in a little longer time. In the coldest winter days with the least solar intensity, the bacilli never withstood two hours of radiation. 2. Ultraviolet rays of the summer sun only harm these bacteria and only in very exceptional cases kill them. This ultraviolet light offers at the most 20 per cent of the total light effect. Those wave lengths between 450 and 280 microns constitute the ultraviolet light. The bactericidal working of sunlight is about proportional to the physical and chemical intensity in which the maximum brightness and photometric effects join in with the greatest disinfecting power. Controls showed that drying and heat had no particular influence upon these results. It is to be assumed that the killing of the bacteria has to do with osmotic changes. It may occur through oxidation, coagulation or the destruction of albumin. It is not finally decided that the favorable healing effect of sunlight has any direct relationship to the bactericidal action of the rays. The hours in which the greatest intensity of ultraviolet light is found are just those of the day during which patients do not take the cure. The importance of the ultraviolet rays in the cure is exaggerated.—*Über die desinfizierende Kraft der Sonnenstrahlen gegenüber Tuberkelbazillen, J. von Bergen, Schweiz. med. Wchnschr., December, 1920, 1120.*

Contribution to the Scientific Study of Heliotherapy and Phototherapy.—Rollier and Rosselet in 1908 attributed their success not only to the ultraviolet rays but to the whole spectrum. They found that the patients who pigmented did better than those who did not. The pigment was considered to be able to change not only the ultraviolets but also the blues and violets into rays of longer length and therefore greater penetration. No satisfactory spectroscopic study of pigment could be made. Most of the enthusiasm for the mercury quartz lamp has resulted from the studies of Berthelot and Gaudechon made in the laboratory of Meudon. They found that under the influence of ultraviolet rays a mixture of CO_2 and NH_3 becomes the amide of formin, which is justly considered the point of breaking off of albuminous substances, and this is the basis of living tissues; also the same rays exposed to a mixture of water and carbonic acid form formaldehyde, the condensation of which gives the vegetable sugars. This was found in the laboratory to be the first stage of assimilation of chlorophyll. Among the heat bodies formed, they were able to produce an explosive gas by exposing water to these very short rays. They obtained this at ordinary temperatures, whereas without the rays it can only be at a temperature of 1000°. All these experiments were obtained only with the extremest of the short ultraviolets. The results obtained in the laboratory in regard to assimilation of chlorophyll are realized in nature by the use of plain sunlight, and this does not contain the short ultraviolets of the lamp. The question as to the exact properties of pigment is unsettled. If one says that it is a protection only, then it can not be considered as a means of using the rays of sunlight more profitably. Von Bergen recently found that bactericidal action of sunlight ultraviolet is only 20 per cent of the total direct sunlight, but he does not decide (nor has any one else) whether the efficacy is due to the intensity or to the frequency of the radiations. From most of the experiments, Rollier concludes that more credit should be given to the light rays because in nature they have a similar effect to that which the ultraviolet rays or the very high temperatures have in the laboratory. All the radiation emitted by the sun can affect our organism.—*Contribution à l'étude scientifique de l'héliothérapie et de la photothérapie, A. Rollier and A. Rosselet, Schweiz. med. Wchnschr., February, 1921, 172.*

Light Dosage.—The need of some method of accurately knowing the intensity of the source of ultraviolet rays led the writer to repeat the work of a few others who claimed that the chemical destruction of a mixture of hydrogen and iodine was a simple and accessible method. The quartz light of Jesionek was used and titration carried out with 1/400 normal sodium thiosulphate solution. A colorimeter that had been recommended to determine the intensity of color of the liberated iodine was also used. The conclusion was reached that the measuring of the workings of the ultraviolet rays through titration and colorimetric methods for the amount of iodine set free was not a practicable nor a simple method and deprived the physician of too much time for controlling the dosage of light treatment.—*Versuche zur medizinischen Lichtdosierung, F. Rettig, Deutsche med. Wchnschr., January, 1921, l, 74.*

Scarlatinal Rash After the Use of Quartz Light.—A patient eighteen years old had, as a child, measles, diphtheria and also possibly scarlet fever but no previous skin diseases. He had always reacted to sunlight with a good pigmentation although a blonde in type. He was exposed to the lamp at a distance of 70 cm. for three minutes in the upper part of his body, front and back. At night, on going to bed, red spots about the size of a ten cent piece appeared on the neck, behind the ears and later on the chest and soon spread all over the body except around the mouth and nose. They could be made to disappear on pressure. After two days the rash began to disappear. There was no rise of temperature and no symptoms in the throat and no general disturbance. No reasonable explanation could be given for this.—*Skarlatinoses Exanthem nach Quarzlampenlicht, H. Austgen, Deutsche med. Wchnschr., January, 1921, l, 75.*

Action of Light on the Leucocytes.—Many conflicting opinions in regard to the action of light on both the red and white cells have been reported. There is considerable evidence for believing that there is a decrease in the red cell count and in the percentage of hemoglobin in the dark but an increase in the light. However these changes are not permanent. The usual opinion in regard to the white cells has been an increase in the lymphocytes and a decrease in the polynuclears as a result of prolonged exposure to sunlight, although this finding is not conclusive. In the present experiment, separate parts of the spectra of the iron arc were used to determine the effects on the blood of rabbits whose ears were exposed for one hour at a distance of ten inches. The ear was shaved and the eyes were covered. The iron arc is almost a continuous source of light and is strong in the ultraviolet, in contrast to sunlight, which is really weak in ultraviolet, but stronger in visible light. Screens were used to allow separate determination of the effect of the short ultraviolets and the longer ultraviolets and two divisions of the visible spectrum. No changes occurred in the red cells. The changes in the white cells were the following: 1. The region of far ultraviolet (wave length shorter than 300 microns) has practically no effect on the absolute number of polymorphonuclears, but produces a very marked lymphocytosis, lasting about three weeks. 2. The near ultraviolet (330 to 390 microns) has a marked depressing effect on the lymphocytes, and, to a less degree, on the polymorphonuclears. 3. The region between 450 and 650 microns has a stimulating action on both lymphocytes and polymorphonuclears, particularly on the former. 4. The wavelengths longer than 650 microns (the red and infrared), produce no effect on the blood beyond the drop in lymphocytes which occurs immediately after exposure to light of any kind. No satisfactory explanation can be given for the cause of these changes. It was attempted to prove that the destruction of the white cells at the start of radiation might act as a stimulus to the lymph nodes and thus cause the subsequent rise, but injection into rabbits could not verify this. Likewise an attempt to prove that the absorption of light by the hemoglobin or plasma of the blood might lead to the formation of products that stimulate the production of lymphocytes failed. The action on skin tissue may be indirectly responsible.—*Action of Light on the Leucocyte Count, Janet H. Clark, Am. J. Hyg., January, 1921, i, 39.*

The Presence of Red Blood Corpuscles in the Miliary Tubercles of the Spleen.—The histologic examination of the spleens from 36 of a total of 46 cases of miliary tuberculosis in man in which this organ was involved in the general process revealed varying grades of accumulations of red corpuscles (hemorrhage) in the tubercles. In 8 of the negative cases the marked necrosis present may account for the absence of red cells in these spleens; only 2 cases thus being definitely negative. The difference between the lymph nodes and the spleen in this respect is explained on the basis of their different anatomical structure especially as concerns the lymphatic and blood vessels, there being no marked differentiation between these vessels in the spleen, while in the lymph nodes they are entirely separated. The spleen is likewise to be considered as anatomically differing in this respect from all the other organs of the body. An inflammatory basis for the presence of the red corpuscles in the tubercles of the spleen is not tenable.—*Über das Vorkommen roter Blutkörperchen in den Miliartuberkeln der Milz, O. Heitzmann, Virchow's Arch. f. path. Anat., 1920, ccxxvii,* 174,

The Endothelium in Experimental Miliary Tuberculosis.—The purpose of this paper is to draw attention to the important part taken by cells originating in capillary endothelium, in various types of inflammation. This is a report of the histogenesis of the cells forming the tubercles produced in rabbits by the intravenous injection of tubercle bacilli. Conclusions: 1. Miliary tubercles produced in the lung, liver, spleen, kidney, lymph nodes, and omentum of the rabbit by hematogenous tuberculous infection are composed chiefly of cells originating in the capillary vascular endothelium. 2. These cells have a marked affinity for carbon in colloidal suspension, which makes their identification possible. 3. A benzidine dye like niagara blue, while acting selectively on macrophages, lymphoid reticular cells, renal convoluted tubular epithelium and free polymorphonuclear leucocytes is not found in the tubercles to any appreciable extent, unless there is necrosis. when the staining is diffuse. 4. The tubercle reticulum is composed of fibrils resembling connective tissue fibroglia and collagen fibers in every way and is produced not only by fibroblasts, but by the endothelial cells themselves, after these have migrated from the vessels, differentiated into epithelioid cells, and formed tubercles. This process is well advanced five weeks after inoculation.—*Studies of Endothelial Reactions. IV. The Endothelium in Experimental General Miliary Tuberculosis in Rabbits, N. C. Foot, J. Exper. Med., February, 1921, xxxiii, 271.*

Hemorrhages into the Liver in Pulmonary Tuberculosis.—Punctate hemorrhages into the liver occur in cases of pulmonary tuberculosis which differ from those occurring in other hemorrhagic conditions (eclampsia, sepsis, etc.) affecting the liver. Meyer and Schoenlank believed them to be agonal and all of the same duration. Mittasch studied the liver from a far advanced consumptive histologically and found evidences of various stages of organization and fibrin formation which led him to the conclusion that the condition is neither agonal nor entirely occurs at the same time. No actually ruptured vessels were found, but he believes ectatic veins or capillaries of toxic or other origin may easily be ruptured by blood pressure changes occasioned by violent coughing in consumptives.—*Über Leberblütungen bei Lungentuberkulose, G. Mittasch, Virchow's Arch. f. path. Anat., September 30, 1920, ccxxviii, 476.*

Anatomic Investigations of Tuberculosis in Childhood.—Postmortem examinations in the pathological laboratory of the University of Utrecht from August, 1906, to January, 1919, of 776 children up to fifteen years disclosed tuberculosis in 187 of the cases, the frequency increasing with age. A few cases were found at birth. Primary intestinal tuberculosis was rarely found anatomically so that aerogenic infection should be looked upon as the usual route. Prophylaxis should begin with the removal of young children from the surroundings of open consumptives. Pulmonary tuberculosis was especially malignant. There were 60 cases of tuberculous meningitis among the 187 cases. Bone tuberculosis, especially of the spinal column, in youth was mild and had a protracted course.—*Pathologiesch-Anatomiesche Onderzoekingen van Tuberkulosis in den Ouderdom van Kinderen, E. C. Rijssel, Geneeskund Bladen uit Klin. en Labor., xxi,* 32 (*translated from Zentralbl. f. innere Med., April 17, 1920, no. 16, 292*).

Tuberculosis Antibodies in the Aged.—In order to confirm the impossibility of diagnosis of clinical tuberculosis by the cutaneous tuberculin reaction, Ichok in the laboratory of Besredka, Institut Pasteur, selected 12 nontuberculous patients from sixty-two to eighty-eight years. Eight were senile, three had nervous affections, one showed symptoms of hemiplegia. The intracutaneous reaction was positive in every case after forty-eight hours. The finding of tuberculosis antibodies by means of the complement fixation test is much more important clinically. In active tuberculosis the fixation reaction is early and very pronounced; in inactive or absent tuberculosis the reaction is negative. Since tuberculosis in the aged usually is in attenuated form, because of increased resistance, it seemed important to undertake a study of the antibodies in them. The study was made on 100 patients cared for at the Salpêtrière and in the hospital St. Louis. There were 20 patients aged fifty to fifty-nine years, 19 from sixty to sixty-nine years, 42 from seventy to seventy-nine years and 19 from eighty to eighty-eight years. Fifty-two of these showed positive signs of tuberculosis and 48 were nontuberculous. Of the 52 patients, 18 had pulmonary tuberculosis, 24 lupus and skin tuberculosis, 6 osteomyelitis and arthritis, 1 Pott's disease and 1 cold abscess. The 48 nontuberculous patients were suffering from senility (21), nervous affections (11), hemiplegia (4), cardiac disease (4), rheumatism (2), tumors (2), arthritis (2) and bronchitis (2). The sera from the 48 nontuberculous patients all gave a negative result. Of the 52 tuberculous cases, 46 gave a positive result. Unrecognized tuberculosis of the aged is particularly dangerous to the environment; hence the value of the reaction. The negative results observed in the patient without clinical manifestation of tuberculosis demonstrate that the antibodies do not remain in the organism after the first infection which almost always occurs in early infancy, but that they are the result or the evidence of actual disease.—*La recherche des anticorps tuberculeux chez les vieillards, G. Ichok, Progr. Méd., January 22, 1921, no. 4, 25.*

Resistance of the Caterpillar to Tubercle Bacilli.—Previous investigations by the same author have shown that as a rule invertebrates are highly resistant to organisms pathogenic for man. Curiously enough the caterpillar *Galleria Mellonella* is much less resistant to injections of certain saprophytes, as B. coli, B. pyocyaneus, B. subtilis, and B. proteus. It displays an extraordinarily high resistance to infection with tubercle bacilli. The latter injected into the body cavity in uniform suspension, in volume equal to the total blood volume, undergo rapid phagocytosis by wandering cells and encapsulation by masses of such cells. Encapsulation occurs within two hours, hundreds of capsules being formed within a day. The capsules persist during the incubation of the caterpillar and its development into chrysalides and butterflies. They are formed in the latter following injection almost as well as in the immature caterpillar. The capsules may be looked upon as true tubercles. Within them the bacilli are digested to a brown, liquid mass, within which acid fast bacilli may not be found, unless they were present in large clumps in the injection mass. Contrary to the results of Fiessinger the author finds that five days after infection the contents of these caterpillars are as a rule not infective for guinea pigs. Thus the caterpillar displays a high resistance to infection with the tubercle bacillus due to intracellular digestion. Serum antibodies could not be demonstrated. Metalnikow was unable to isolate the ferment responsible for the intracellular digestion.—*L'immunité naturelle et acquise chez la chenille de Galleria Mellonella, S. Metalnikow, Ann. d. l'Inst. Pasteur, November, 1920, xxxiv, 888.*

Metabolism in Grave, Afebrile Tuberculosis.—From a practical standpoint it is important to know whether in afebrile tuberculosis there is an increase in the metabolism of the whole body in much the same manner as in carcinoma and in leukemia. On the basis of his observations over a period of years the author feels himself in a position to decide the question. A table gives the results of his investigations in ten afebrile, very active, progressive, open, cases of tuberculosis. Of these ten only two showed no increase in metabolism, in one the increase was very slight, while the others presented increases of from 20 to 36 per cent. He concludes that the gross calory requirement in severe, progressive tuberculosis, with the patient in bed and suffering from no marked dyspnea, no matter whether there is moderate or no fever, is from 50 to 55 calories per kilogram of body weight, or about 1500 calories per square metre of body surface. In cases with high fever, from 60 to 65 calories per kilogram, or about 1700 calories per square metre are required for really adequate nutrition. In practice it may not be always possible to attain this standard, but we must strive for this goal.—*Stoffwechsel Untersuchungen bei schweren afebrilen Tuberkulosen, E. Grafe, Münch. med. Wchnschr., September 17, 1920, lxvii, 1081.*

Metabolism in Tuberculosis.—In regard to the dietary of tuberculous patients medical opinion has fluctuated within wide limits. To make the selection it is necessary to know the total energy transformations in such patients and the extent of destruction of protein by the toxins of the disease and the minimum amount of protein which must be given to maintain the patient in nitrogen equilibrium. In this study the respiration calorimeter of the Russell Sage Institute of Pathology was employed. Fifteen patients in all stages of the disease and with various complications were studied 14 to 16 hours after the last regular meal. It was found that the basal metabolism of tuberculous patients may be normal or very slightly above that of normal men of the same size. Thus, in 10 cases the variations from average normal was from minus 3 to plus 15 per cent. Further increases in metabolism occur with a rise of body temperature. These increases are not large. Thus, in one case the temperature rose 1°C. during two hours without a chill and the heat production of the second hour was only 2 calories greater than that of the first hour. With a rectal temperature of 104° F., the metabolism may be 30 per cent above the average normal. The basal heat production in tuberculosis may be less than the normal for the same patient when in health; in other words, the loss in weight may be accompanied by a reduction in metabolism which more than compensates for the tendency to increase caused by the disease. Limited data regarding the nitrogen excretion show that, while a toxic destruction of protein does exist in tuberculosis, it is not large. The urinary nitrogen may be reduced to from 5 to 6 gm. per diem, though nitrogen balance may be attained only at a higher level (about 10 grams a day). The specific dynamic rise in metabolism produced in 2 cases by the ingestion of a protein meal corresponded closely with that produced by the same meal in 3 normal men. Conclusions: In view of the fact that the food requirements of tuberculous patients are not large, either as regard total energy value or nitrogen content, forced feeding is unnecessary and is probably harmful in the active stages of pulmonary disease. Since protein increases the respiratory exchange in the tuberculous as in the normal, it may be well to limit the protein intake during periods of activity of the disease in order to put the lungs at rest. —*Clinical Calorimetry. XXIX. The Metabolism in Tuberculosis, W. S. McCann and D. P. Barr, Arch. Int. Med., December, 1920, xxvi, 663.*

Metabolism and Diet in Tuberculosis. —In the management of tuberculosis dietotherapy has long occupied a place of primary importance, perhaps justly, since none of the more specific therapeutic measures, including tuberculins of diverse sorts, vaccines, serums or drugs, have gained paramount significance. A recent writer has reëchoed a widespread belief by stating that beyond possible doubt food, good food, properly chosen, properly prepared and eaten in cheerful surroundings is our sheet anchor in this disease. Yet a survey of current proposals reveals widely divergent views as to how the tuberculous may best be nourished. As if overwhelmed by the thought of consumption, some clinicians have advised an ultraliberal intake of food for the patients almost regardless of the digestive disturbances which ill considered dietary measures may readily provoke. It is related that Debove, having discovered by accident not only that gastric lavage arrested the vomiting of phthisical patients but also that food introduced through a tube could be retained and digested, proceeded to disregard the anorexia of tuberculous patients, and fed them with extreme liberality. A system of superalimentation involving the use of literally enormous, concentrated diets found considerable vogue for some time until a reaction set in against it. Other vagaries of treatment concerned the proportion of protein to be included in the diet. Again, fats, particularly cod liver oil and egg yolk, claimed prominence in the directions to the afflicted. Summarizing the practice in nearly a hundred leading sanatoriums of the world in 1908, Irving Fisher stated that the total calories fed ranged from a maximum of 5500 to a minimum of 2140, the intake of protein varying from 60 to 90 grams a day. The study of metabolism has meanwhile advanced to a stage which makes it possible to ascertain with scientific accuracy whether undue demands for energy are made on the body during the progress of tuberculosis. Calorimetric investigations of the metabolism in fever have left no doubt as to the large toll which this abnormal condition levies on the body's store of nutriment. As a consequence the dietetic treatment, notably in the case of typhoid fever and other conditions has been beneficently modified in the direction of liberality. It is high time that an equally rigorous analysis be applied to metabolism in tuberculosis, so that the physician may be intelligently guided in the prescription of suitable diets for his patients. Thanks to the contributions by McCann and Barr from the Russell Sage Institute of Pathology at Bellevue Hospital, New York City, some dependable facts are at length available. From these it appears that the basal metabolism of tuberculous patients may be normal or slightly above that of normal men of the same size.

Thus, in ten cases, the variation from the average normal was from minus 3 to plus 15 per cent. Further increases in metabolism occur with a rise of body temperature. These increases are not large. Thus, one case is reported in which the temperature rose 1°C. during two hours, without a chill. The heat production of the second hour was only two calories greater than that of the first hour. With a rectal temperature of 104° F. (40°C.) the metabolism may be 30 per cent above the average normal. The basal heat production in tuberculosis may be less than the normal for the same patient when in health; in other words, the loss in weight may be accompanied by a reduction in metabolism which more than compensates for the tendency to increase caused by the disease. One would expect some toxic destruction of protein in any febrile disease. At most, however, it is not large in tuberculosis. McCann and Barr venture to believe that many febrile tuberculous patients may be kept in nitrogen balance on diets containing from 60 to 70 grams of protein each day. This amount is much less than Voit's standard allowance (118 grams) for normal men, though somewhat greater than the normal minima of Chittenden and of Sherman (from 35 to 45 grams). It is much less than is fed to patients in many of the sanatoriums for tuberculosis. Consequently, forced feeding and high protein diets are unnecessary if not actually harmful in the active stages of pulmonary disease. In fact, the increased metabolism necessitated by overliberal food intakes leads to an increment of respiratory activity at a time when pulmonary rest is quite as much indicated as is muscular rest. In furnishing specific data, the New York investigators conclude that during periods of activity of a pulmonary tuberculosis the diet need not contain more than 500 calories above the basal requirement (from 2000 to 2500 calories), nor more than 60 grams of protein. The object of such a diet is to maintain the respiratory activity at the lowest level compatible with the maintenance of nitrogen equilibrium. There are losses of protein in the sputum, but according to Lanz they are not likely to exceed 7 grams a day. Muscular work, of course, calls for an added supply of energy. Accordingly, when the activity of the disease has subsided, the total calories in the diet should be raised to meet the requirements of the patient as his muscular activity increases. On the basis of these findings it should not be difficult to epitomize the dietotherapy of tuberculosis more successfully than ever before.—*Editorial, J. Am. M. Ass., February 26, 1921, lxxvi*, 592.

Misleading Beliefs Regarding Pulmonary Tuberculosis.—The first of these beliefs concerns râles as an evidence of active or unhealed pulmonary tuberculosis. They do not call for special treatment unless there is other evidence of active disease. If there is no evidence of tuberculous toxemia such as increased afternoon temperature, rapid pulse, cough with expectoration and loss of weight and strength, then the râles indicate only what has been and not what at the time exists. It is not an unusual occurrence to observe a patient who has for many months lost all his symptoms, presenting every evidence of perfect health and able to pursue his usual duties, still showing râles over the area of the localized disease and these râles may persist for months or even years. Conclusions: 1. Râles alone do not prove active tuberculosis and may remain an indefinite time after the lesion has healed. 2. When tubercle bacilli have been demonstrated in the sputum it has been generally considered that the carrier is actively tuberculous and should be placed under active treatment. It has been found that certain healthy persons, when from one cause or another they have had their sputum examined, have shown tubercle bacilli. Why should not there be tubercle bacilli carriers as well as typhoid and diphtheria carriers? Tubercle bacilli in the sputum with no other symptoms does not mean active tuberculosis. One may have them for years without disease. 3. There is still too much dependence placed upon the detection of definite physical signs, the finding of tubercle bacilli in the sputum and the result of the X-ray examination in making an early diagnosis. If symptoms of toxemia are present it is unmistakable evidence that active tuberculous infection exists. An early diagnosis must as a rule be made upon the symptoms of tuberculous toxemia; physical signs may or may not be present. 4. Undue fear of the communicability of pulmonary tuberculosis from one adult to another is unwarranted in the present state of our knowledge and there is much evidence for the belief that it never occurs. 5. The open air treatment must be applied with judgment and climate alone will not cure a tuberculous individual. 6. In the treatment of pulmonary tuberculosis there is a time for exercise as well as rest, but one must wisely choose the time for the former and skilfully direct it.—*Some Misleading Beliefs Regarding Pulmonary Tuberculosis, E. O. Otis, Milit. Surgeon, February, 1921, xlviii, 159.*

Latent Pulmonary Tuberculosis in Its Disguises.—The term latent pulmonary tuberculosis is used for those cases of tuberculosis of the lungs in which there is no cough. The symptoms the patients complain of may be divided into the nervous, autonomic, gastrointestinal, asthenic, rheumatic, dermatological, cardiac, menstrual, and general groups. The author has never seen a latent case in either of the sanatoria with which he has been connected. An analysis of 75 of his private patients exhibiting pulmonary consolidation without suffering from cough is made: 24 were males and 51 females; 4 were ten years of age or younger, 13 between eleven and twenty, 29 between twenty-one and thirty, 16 between thirty-one and fifty, 7 between forty-one and fifty; the age was not recorded in the rest. One was in the far advanced stage, the rest were incipient or first stage cases. Thirty-two gave a family history of tuberculosis. Sixty-three of the patients complained of nervous symptoms, 52 of pains, 41 of autonomic phenomena, 35 of gastrointestinal disturbances, 28 of menstrual disorders, 16 of skin eruptions, and 67 of asthenic, cardiac, general and other symptoms. The chief nervous symptoms were nervousness, depression, insomnia, irritability, excitability, restlessness, tremors, hysteria, twitching, nervous prostration, disagreeableness, mental tire, and nausea or vomiting accompanying headache. Of the pains complained of, the most frequent were headache, backache, pain in the legs, precordium, chest, back of the neck, abdomen, sacroiliac joint, shoulder blade, supraorbital region, arm and shoulder. The autonomic phenomena most frequently met with were dermographia, pallor, tricolored finger nails, sweating exclusive of night sweats, flushing, showing of sclera above or below the cornea on opening the eyes widely, subjective sensation of cold, migraine, bleedings exclusive of hemoptysis, urticaria, the leaving of a black line when a silver probe is drawn across the face, showing of sclera normally above or below the cornea, feeling worse in hot weather and better in cold weather, and nosebleed and angioneurotic edema. The chief gastrointestinal symptoms complained of were nausea, eructation, vomiting, epigastric pressure, smothering, lump, weight or heaviness, epigastric pain, pyrosis, abdominal pain, sour taste, nervous indigestion, heartburn and distention. The most common of the menstrual and pelvic disorders were dysmenorrhea, exacerbation of other symptoms during the menstrual period, irregular menstruation and menorrhagia. Of the symptoms classed as general those most frequently complained of were weakness, tendency to tire easily, being always tired, malaise, dyspnea and palpitation on exertion, vertigo, anorexia, loss of weight, failure to gain weight, dyspnea, listlessness, languor, lack of ambition, constipation, exhaustion, sore throat, hemoptysis, lessened appetite, fainting and frequent urination. As a rule the symptoms described do not subside on symtomatic or ordinary treatment. Tuberculin is seldom of value. Proper hygiene, fresh air, good food. sufficient rest, proper exercise, hydrotherapy, and Bier's hyperemia of the lungs and bone marrow are always indicated; some cases retain their symptoms in spite of every method of treatment. The therapeutic agents that seemed to be of most benefit were iodoform in doses of one-eighth grain, increased gradually to a grain, iron, arsenic, strychnine, picrotoxin, digitalis, valerian, and calcium glycerophosphate or lactophosphate. Many of the symptoms mentioned doubtless have no connection with the tuberculous process. It is possible that some may be produced as a direct result of the body's fight against the tubercle bacillus and its toxins.—*Latent Pulmonary Tuberculosis in Its Various Disguises, M. Solis Cohen, N. York M. J., January 22, 1921, cxiii, 144.*

Chronic Pulmonary Tuberculosis with Few Symptoms.—Four cases are described in which physical signs were meagre, but in which the X-ray showed disseminated pulmonary foci. The usual symptoms were mostly lacking. Dyspnea on exertion was usually present, fever was slight or absent and tubercle bacilli appeared late. The course of the disease is chronic, the prognosis is bad.—*Zur Kenntnis der symptomarmen, wahrscheinlich auf dem Blutwege enstandenen Formen der chronischen Lungentuberkulose (zerstreute, kleinherdförmige Tuberkulose), G. Bolle, Ztschr. f. Tuberk., October, 1920, xxxiii, 32.*

Symptoms vs. Physical Signs in Early Diagnosis.—Brown has shown from his experience at Trudeau that out of twenty-eight per cent of their patients, which were incipient, came 69 per cent of their apparent cures. Gilbert is convinced from a study of the literature and of his own records that the family focus is the most potent one in the dissemination of infection. If we go very carefully into the family history of our patients, we will find in a large proportion of them that some relative or other, who has lived in close contact with the patient in childhood or adolescence, had chronic bronchitis, a throat cough, or a stomach cough. Gilbert went to the trouble of tracing these contacts and was surprised how almost uniformly they proved to have old fibroid tuberculosis, not very virulent, but ample for the purpose of infecting young persons in the family. Physical signs are usually overemphasized and not enough weight is attached to symptoms in early diagnosis.—*Symptoms vs. Physical Signs in the Early Diagnosis of Pulmonary Tuberculosis, O. M. Gilbert, Med. Herald, January, 1921, xl, 25.*

Tenderness Over Tuberculous Apex.—Sabourin, in 1910, drew attention to the value of examining with the finger tip for circumscribed tenderness along the intercostal spaces anteriorly, at the bottom of the supraclavicular triangle, and in the supraspinous fossa; where the pain on pressure is elicited the patient withdraws his shoulder or exhibits a localized muscular contraction. Pressure should be made gently, gradually, and systematically, so as to cover every portion of the suspected areas. The tenderness on the affected side contrasts with the lack of sensitiveness on the sound side. The presence of actual tenderness distinguishes active from quiescent tuberculous lesions. The author, examining a large number of cases, found the local tenderness constantly present in tuberculous patients and absent in others. In 192 consumptives with tubercle bacilli in the sputum tenderness at the midpoint of a line drawn from the base of the neck to the acromion was always present, being especially marked during acute exacerbations of the disease, and less pronounced at other times, yet persisting for a considerable period, even after disappearance of the auscultatory signs of the disease. In four patients with cavities, who had recovered under sanatorium treatment and whose sputum was free from bacilli, tenderness was absent. In one case in which a patient had been worried because of loss of weight and had a tender point the physician, finding auscultation negative, ascribed the tenderness to a neuropathic state and ordered hydrotherapy; a week later, a copious hemorrhage, with fever and definite signs of tuberculosis showed the true condition of affairs, which had already been manifested in the tender point. Tenderness in the intercostal spaces and in the axilla was elicited in one half of all cases and tenderness above the clavicle in four-fifths of the cases. Besides revealing active lesions, the tender points indicate recovery when they disappear—especially when they do not return with intercurrent febrile disturbances—and constitute the best guide available to the physician for regulating the treatment and prolonging, reducing, or stopping the rest cure. Coupled with supraclavicular adenitis, the points of tenderness assist in the making of an early diagnosis of tuberculosis.—*La douleur locale à la pression du doigt et les adenites sous-claviculaire chez les tuberculeux, G. H. Lemoine, Bull. d. l'Acad. d. Med., November 30, 1920, lxxxiv, 269.*

Apical Respiratory Insufficiency and the Diagnosis of Pulmonary Tuberculosis in Adults.—As Sergent of Paris has recently remarked, there exists quite a large category of pseudo-phthisical subjects. He calls these by the apt term of cases of respiratory insufficiency. The diagnosis is especially necessary when respiratory insufficiency, instead of being complete, is exclusively confined to the apices. In these circumstances, the localization of the physical signs, becoming added to some somatic characters and a few general symptoms, should the examination be insufficiently methodical, there may result a mistaken diagnosis. Cases of this kind are fairly frequent in practice and it is therefore essential to insist upon the symptomatic characters which specify this syndrome. The syndrome is invariably bilateral and purely functional, whereas respiratory insufficiencies, the result of lesions, are usually confined to one lung. The condition is particularly met with in adults. The physical syndrome is the consequence of a decreased ventilation of the apices and makes itself manifest essentially by a decrease of sonority, vocal vibrations, vesicular murmur, amplitude of the respiratory movements, the absence of adventitious sounds, rough breathing, and souffle. Besides these signs, the various means of exploration concur in showing that the apices, although in a state of functional respiratory insufficiency, preserve the possibility of becoming momentarily sufficient, and this is precisely because no lesion exists that can hinder their ventilation and expansion. The measures of functional capacity—spirometry, plessimetry—estimate the degree of the insufficiency. To this functional disturbance more or less accentuated general symptoms become added, which are just the ones that lead *a priori* to a suspicion that the condition may be tuberculosis, because of the insufficiency of weight and musculature, general hypotony, anemia and anhematosis, all of which attain a much more accentuated degree when total respiratory insufficiency complicates the insufficiency at first confined to the apices. The majority of these patients are young, but the syndrome may sometimes be met with in subjects over forty years of age. Almost all have had adenoids in the past and have been operated on some time previously, or else the nasal fossæ are impermeable so that they have lost the habit of breathing normally and no longer ventilate the lungs properly. Now, if this insufficient ventilation is at first confined to the apices it is because the apex is the region of the lung which in normal condition is the least ventilated. The primary cause of this diminished ventilation of the apices, according to Sergent, should be looked for in insufficiency of movement of the diaphragm. In cases of injury of the base of the thorax, especially those of warfare, one can very distinctly see with the fluoroscope that the apex—considering only intact apices—has a lesser transparency and expansion although preserving the possibility of offering the characters of a well ventilated apex when the patient is made to cough. On the other hand, in patients with nasal obstruction the diaphragm moves poorly. Therefore the mechanism of the syndrome of respiratory insufficiency of the apices, which is above all met with in subjects offering inadequate nasal respiration, is clearly explained, and it can readily be conceived why, if the diaphragmatic disturbance becomes extreme, total pulmonary insufficiency becomes installed, overshadowing the apical insufficiency which becomes only a localization. The diagnosis of this syndrome is fairly easy when it is well known. Its bilaterality prevents confusion with insufficiencies due to apical lesions and bilateral apical sclerosis is practically the only morbid process for which it might be mistaken. But the physical signs and X-ray findings are very different in the latter process. The absence of adventitious sounds and the perfect regularity of the respiratory sounds in both apices will prevent any diagnostic mistake. The prognosis depends upon the treatment employed. If this condition is allowed to continue it will inevitably react upon the general health because the somatic characters of the process are rather the effect than the cause of the functional disturbance. The treatment consists of respiratory reëducation and gymnastics methodically and progressively carried out.—*Editorial, Med. Rec., February 12, 1921, xcix, 271.*

Presumption of Tuberculosis From External Stigmata.—Queyrat interests himself in the old-fashioned methods of diagnosis from deduction. Hs enumerates the slenderness of the long bones, the defective development of the musculature and especially that of the thorax, where there is actually atrophy of some of the muscles, which appears to result from the presence of a focus of disease in the apex of the affected side. However, in the case of these petty signs it is not always possible to distinguish between the candidate for phthisis and the early victim. Atrophy of the trapezius, great pectoral, etc., is one of the presumptions that a focus is already present. Percussion myoidema of phthisiologists is an induced phenomenon in the same muscles. But it should be borne in mind that myoidema is common to cachexias and is without specific significance. Pectoral myoidema (or myedema) was extremely common in an epidemic of cholera in 1885. It is common also in cancerous cachexia. Winglike scapulæ are due to atrophy of the serratus magnus and is seen in candidates and even in those who do not seem predisposed to the disease. Tall and slender subjects of the so called "poplar" type are to be classed as candidates. The author mentions in passing the facies amabilis of old clinicians—with its long oval, its mobility, its thick eyebrows, long lashes, and bluish sclerotics. The eyes are especially languishing and beautiful. Chlorotuberculosis is a special form, with various hypoplasias, including those of the genitals, which is said to be readily curable. Of other petty signs the author enumerates thickish skin, lively blush on the cheeks, thick lips, wide nose, chilblains, fissures between the cheeks and lobule of the ears, deceptive appearance in plump subjects because of good nutrition, high color, and clear eyes. Hippocrates, who presumably lived among a population containing a large percentage of dark-complexioned peoples, laid emphasis on red hair, clear skin, and blue eyes as predisposing to phthisis. But it is not so much the exclusively rufous subject who seems to invite the disease, for brunettes of the erythic type suffer equally with the blondes and rufous. That is, in tuberculous subjects we often find a hybrid between brunette and red, as when black head hair is associated with red beard or pubic hair. Hirsute subjects, when this trait is not associated with the cave man proportions, are very suggestive of phthisis. This is shown in an old Latin maxim—a hairy man is either strong or consumptive. Rather suspicious in girls are plump mammæ with general lack of adipose. Smallpox scars in a subject suggest the old dictum that the victim of variola very often dies of or with tuberculosis, as shown by autopsy findings. Scars of old scrofula, scar keloid, and perhaps spontaneous keloid are all suggestive of tuberculosis, past or future. The author concludes with a long parade of the so called paratuberculous dermatoses which have gradually increased in numbers to such an extent that they are often the only evidence which points to the disease.—*Editorial, Med. Rec., January 8, 1921, xcix, 61.*

The Drooping Shoulder Sign.—Of the last 50 cases seen by Rivers there has been present in 25 cases a sign not mentioned in British text books. On the affected side or (generally) the side of more extensive or older disease, the points of the shoulder and the nipple are lower than on the other side. The nipple is also smaller and seems to lie further back. Behind, the scapula is lower, its inferior angle may reach three inches below that of its fellow, and is at a different distance from the spine, usually nearer to it. Muscular atrophy also is noticeable, a little of the pectorals, but more of the upper part of the trapezius. The superior border of that muscle is flattened, wasted, hollowed out so that, as compared with the opposite side, much less of it shows above the clavicle when viewed from the front and above the spine of the scapula when viewed from behind. The sign is more marked in men and occurs in a rather large proportion of juvenile hilum cases. It occurs in very nearly half of the third stage cases, in nearly half of the first stage and in about a quarter of the second stage cases. The author saw it develop in the course of a few weeks. The sign is almost certainly tuberculotoxic in origin. It is clear, objective and definite, and of great practical value, especially in children's phthisis, and in chronic bronchitis, complicated by a small patch of tubercle.—*The Drooping Shoulder Sign of Phthisis, W. C. Rivers, Brit. M.J., January 22, 1921, 120.*

Significance of Slight Fever in the Tuberculous.—When the rectal temperature shows a rise to 37.7° or 38°C. (100.4° F.) after an hour's walk, this suggests suspicion that something is wrong but it by no means testifies to tuberculosis, not even when the temperature goes still higher than this. Individual habits must also be considered; a letter carrier would react differently from an office clerk. Half an hour of repose after the test exercise should bring the temperature down to within three-tenths of a degree Centigrade of what it was before the walk. [Three-tenths of a degree Centigrade is nearly six-tenths of a degree Fahrenheit.] If the temperature takes longer than this to decline, it is strongly suspicious of serious pathological conditions, and tuberculosis is usually responsible. On the other hand, the lack of a temperature reaction is not an infallible sign that conditions are normal. When the thermal reaction to exercise is approximately normal in the tuberculous, this testifies that the focus is more or less healed and isolated. Abnormal fluctuations in the temperature during repose, even if the rise is very slight, demand strict enforcement of repose. This point is the one most often neglected; either the rise is overlooked or is regarded as too slight to be heeded. The author has seen hundreds of patients die from the progress of their disease because the slight rises in temperature during the early, curable stage had not been heeded. Physicians must realize that it is just as wrong to allow patients with even a slight rise in temperature to go for a walk or to work, as for a surgeon or obstetrician to neglect asepsis. The author records the temperature every two hours at first to ascertain the individual type, also the monthly type in women. The temperature is taken several times a day in the febrile and from once to three times in the afebrile, then gradually only once in two, three or seven days, interposing an occasional day in which the temperature is taken oftener. These conclusions are drawn from Voornveld's own observation and experience, but are sustained by literature which he cites.—*Die Bedeutung leichter Temperatursteigerung bei Lungentuberkulose, H. J. A. van Voornveld, Schweiz. med. Wchnschr., June 24 & July 1, 1920, l, 539 & 567.*

Statistics of the Pirquet Reaction.—The figures reported were collected from the records of the Children's Hospital, Philadelphia, for the past ten years. The technique employed was the regulation denudation with the Pirquet borer and immediate application of one drop of pure tuberculin (O. T.). Twenty-seven patients were found to be tuberculous at autopsy. Of these, 16 had given positive and 11 negative reactions. Apart from the fact that only one retest was done in 10 of the 11 nonreacting cases, the high percentage of negative results must have been dependent in large part upon the stage of the disease at the time the test was made. Of the 11 negative results, 8 were obtained in children who died within two weeks. Another patient, not included in the 27, gave a positive Pirquet reaction and was diagnosed pulmonary tuberculosis antemortem, but no lesions of tuberculosis were demonstrated at autopsy. This result cannot be accepted as an authentic instance of lack of specificity of the tuberculin reaction. The autopsy was done by one of the residents, presumably during an emergency and histological examinations were not made. Of 185 retested children 6.5 per cent were tuberculin sensitive only on the second test. The difference in positive results, where the intracutaneous method is used in retesting, as compared with a second Pirquet, hardly seems great enough to compensate for the much more complicated technique of the former method. From a comparison of the clinical and postmortem diagnoses certain facts may be emphasized: 1. The clinical designation of generalized tuberculosis with meningitis depends upon the terminal meningeal infection. 2. Generalized tuberculosis, without meningitis, usually is diagnosed as a pulmonary disease, because of the extent of the pulmonary involvement. As the tuberculin test is of clinical value only in the first years of life, and sputum is difficult or impossible to obtain, where the involvement of the lung consists chiefly of miliary tubercles, there is some justification for error. 3. The distinction between infantile atrophy, chronic gastroenteritis and nontuberculous bronchopneumonia on the one hand, and pulmonary tuberculosis on the other, may, at times, be extremely difficult in the presence of a negative tuberculin test. Repetition of the latter should reduce the percentage of error. 4. Unless the history and course be typical of the type, the possibility of spondylitis should always be considered in the differential diagnosis of a spinal paralysis. This series demonstrates the high percentage of tuberculous infection and the comparatively low incidence of recognizable clinical tuberculosis in childhood. Additional evidence is adduced to prove that a positive tuberculin reaction does not occur in the absence of tuberculous infection. There should be at least one repetition of the tuberculin test if the first was negative.—*Statistics of the von Pirquet Reaction, J. C. Gittings and J. D. Donnelly, Arch. Pediat., February, 1921, xxxviii, 78.*

Diagnostic Value of Intracutaneous Injection of Patient's Own Urine.—From a study of forty children the authors cannot confirm the statements of Wildbolz in every particular but think the method is worth using. In order to form a correct judgment in regard to the relationship between allergy in the individual and the reaction produced by the tuberculin-like substance in the urine, they made control tests in the case of most of the children. In one group of children they injected the urine of other, nontuberculous patients who had shown no reaction after the injection of their own urine. They also applied the urine test to other anergic and allergic children, using the urine of markedly tuberculous children, so that a large percentage of the children, some of whom were known to be allergic and some of whom reacted positively to their own urine, were also tested as to their behavior toward the urine of other children. All the children with a negative Pirquet reaction and without a frank tuberculous focus were found, on examination, not to have the tuberculin-like substance in their urine. Children who reacted to tuberculin were injected with the urine of these children and likewise showed no reaction. When these nontuberculous children were injected with the urine of frankly tuberculous patients they likewise gave no positive reaction. They regard the behavior of children so examined as furnishing proof of the specificity of the urine reaction. Further investigation, however, showed that the urine reaction of Wildbolz does not furnish an absolute criterion in regard to the activity of a tuberculous focus.—*Eigenharnreaktion nach Wildbolz bei tuberkulösen Kindern, Eliasberg & Schiff, Monatsschr. f. Kinderheilk, October, 1920, xix, 5.*

Diagnostic Artificial Pneumothorax.—Fishberg reports three cases of pulmonary neoplasm in which he induced artificial pneumothorax for the purpose of settling the diagnosis. In view of the harmlessness of the procedure, it appears that it should be utilized for diagnostic purposes in all doubtful cases. While most tumors can be diagnosed merely by a careful study of the history and physical signs of the cases, this procedure of diagnostic pneumothorax will in many cases, especially those with pleural effusions, clear up the diagnosis promptly and decisively. It is doubtful whether it is advisable to induce a pneumothorax in cases with aneurysm.—*Discernment of Intrathoracic Neoplasms by Aid of Diagnostic Pneumothorax, M. Fishberg, J. Am. M. Ass., February 26, 1921, lxxvi, 581.*

An Early Diagnostic Sign in Basilar Meningitis.—This diagnostic sign of early meningitis is called a reflex strabismus. It is elicited by flexing the head on the chest. When this is done either a bilateral or unilateral strabismus develops which will last as long as the head is kept flexed and disappears as soon as the head is relaxed. In many cases the strabismus is accompanied by a retraction of the upper eyelids. A contraction of the pupils is also noticed in some cases. During a period of seven years of observation "reflex" strabismus was present in the early stages of almost every case that came under observation. In the late or paralytic stage flexion of the head fails to produce strabismus. By means of this sign one is able to make a diagnosis of basilar meningitis days before any other meningitic symptom appeared. The difficulty of making a positive diagnosis of tuberculous meningitis in the early stages of the disease is well known. In most cases onset is gradual, and the symptoms are vague and indefinite. There may be no other sign than those of vague digestive disturbance for days or weeks. The diagnosisis especially difficult in young infants since the yielding cranium keeps the intracranial pressure below the fatal limits and often weeks will pass before definite signs appear.—*An Early Diagnostic Sign in Basilar Meningitis, D. Gingold, Arch. Pediat., January, 1920, xxxvii, 19.*

Chemical Examination of the Cerebrospinal Fluid in the Diagnosis of Tuberculous Meningitis.—A chemical examination of the cerebrospinal fluid may yield valuable results in cases in which the cell content of this fluid or the general clinical picture may prove misleading. Thus, in a child convalescing from whooping cough and seized suddenly with convulsions and other evidences of meningitis, lumbar puncture yielded a clear fluid with lymphocytosis, reduction of albumin, and a marked excess of sugar. Two days later, the fluid showed improvement and on the fourth day the fever and meningeal signs passed off. On the other hand, in a similar case of meningeal syndrome appearing during recovery from whooping cough, the cerebrospinal fluid showed, aside from lymphocytosis, an excess of albumin and absence of sugar. The child died, and postmortem examination showed tuberculous meningitis. Another child of eight years had fever, headache, vomiting, and constipation one week before admission to hospital. Examination revealed a positive Kernig, but normal reflexes and merely slight photophobia and headache. On lumbar puncture the fluid issued without pressure and after prolonged centrifugation yielded only one lymphocyte in ten microscopic fields. Chemical examination, however, revealed an excess of albumin and only traces of sugar. Similar results were obtained three and eight days later, and meanwhile distinct clinical evidences of meningitis appeared. At the fourth examination there was marked lymphocytosis; the child died the next day, and the autopsy showed tuberculous meningitis.—*De l'utilité de l'examen chimique du liquide cephalo-rachidien dans le diagnostic de la meningite tuberculeuse, G. Mouriquand & Morenas, Lyon Méd., December 10, 1920, cxxix, 990.*

Roentgenography of Obscure Bone Lesions.—In soft tissues it is known that the tubercle bacillus can duplicate the reaction of almost any type of pathogenic bacterium. In tuberculosis of bone, as in soft tissues, there may occur (1) exudative, fibrinous or puriform, (2) discrete proliferative lesions, and (3) a diffuse proliferative reaction, following the exudative, which is essentially tuberculous granulation tissue, with much or little caseation. In the latter instance, there may be new bone formation just as in the repair of pyogenic processes, at a time when destruction or resorption of bone is going on. The important lesson from the pathological study of this series of cases is the reminder that tuberculosis in bone may simulate any other infectious process in location and character of the lesion. Diagnosis from X-ray studies alone is therefore occasionally impossible and recourse must be had to other clinical evidence, and when possible to pathological examination.—*Roentgenographic Appearance, Diagnosis, and Pathology of Some Obscure Cases of Bone Lesions, R. W. Lovett and S. B. Wolbach, Surg., Gynec. and Obst., August, 1920, xxxi, 111.*

Tuberculosis of the Lachrymal Glands.—A survey of the literature and report of two cases from the Jena Eye Clinic is given. In both cases the glands were extirpated.—*Über Tuberkulose der Tränendrüse, W. Stenzler, Dissertation, Jena, 1919 (translated from Internat. Centralbl. f. d. ges. Tuberk. Forsch., August, 1920, xiv, 232).*

Primary Tuberculosis of the Thyroid.—Although the early history in the case was suspicious, tuberculosis had never before been diagnosed. Careful examination of the patient to this time had failed to show any active foci of tuberculosis elsewhere in the body. The history was negative, except for several attacks of tonsillitis and a discharging sinus over the thyroid in earlier life. This showed first at ten years of age and healed after draining for a year At about twelve years of age, it again discharged and continued to do so until the patient was fifteen, when it finally healed and gave no further trouble. About nine months before the authors saw the patient, there began an enlargement of the thyroid. There were no symptoms of hypothyroidism or hyperthyroidism, and the condition appeared to be a simple goitre. The gland was removed and was considered malignant. Gradually the clinical signs of myxedema appeared. The basal metabolism was — 23 per cent, and the patient was given 1 grain of thyroid extract three times daily. This was given four days, when the metabolism was — 6.3 per cent and — 8.4 per cent on successive days. At the end of a month's time the basal metabolism was + 6 per cent. The observation that basal metabolism was lowered before any signs of myxedema developed gives an added interest to metabolism readings in all cases of thyroid involvement, even though the case seems to be only simple goitre. The lowering of approximately 20 per cent in the basal metabolic rate, both before and after operation and treatment, is interpreted as showing practically entire lack of thyroid tissue in the gland at the time of the first examination.—*A Case of Tuberculosis Primary in the Thyroid, W. H. Rendleman and J. I. Marker, J. Am. M. Ass., January 29, 1921, lxxvi, 306.*

Conglomerate Tuberculosis of the Heart.—Tuberculosis of the myocardium is rare. Since 1885, 115 cases have appeared in the literature. The case reported is in a one and one-half year old child with widely disseminated tuberculosis and conglomerate tubercles of the right ventricle.—*Über einen Fall von Konglomerat-Tuberkulose des Herzens, W. Doermer, Dissertation, Jena, 1918, (translated from Internat. Centralbl. f. d. ges. Tuberk. Forsch., August, 1920, xiv, 241).*

Tuberculosis of Myocardium.—The patient had tachycardia, enlargement of the heart and an accentuated second sound in the pulmonic area. Later the heart sounds were both rapid and irregular. Two months before death he developed a temperature reaching 100° F. The urine had a slight amount of albumin. He had a history of syphilis, and the blood gave a positive Wassermann reaction. He became progressively worse, and died six months after admission to the hospital. Both auricles were extensively affected, especially the right one, where the wall was 1 inch thick, due to the caseous material. The tuberculous tissue projected into the auricle, though it did not penetrate the endocardium, and also projected slightly into the upper part of the ventricles. The myocardium near the apex of the heart showed invasion from tuberculous pericarditis.—*Case of Tuberculosis of Myocardium, W. W. Adamson, J. Pathol. & Bacteriol., December, 1920, xxiii, 399.*

Tuberculosis and Cancer of the Lung.—The author reports two cases of combined pulmonary tuberculosis and primary carcinoma of the lung. In both cases cancer developed in the presence of active tuberculosis. The first patient entered the hospital for advanced tuberculosis. Physical signs revealed abscesses at the right upper lobe. The patient was coughing up profuse purulent sputum containing acid-fast bacilli, and complained of excessive pain in the right side. During the course of the disease rather unusual symptoms developed. There was edema of the face; the veins of the chest, upper thorax, and right arm became distended. A diagnosis was made of obstruction to the superior vena cava. Autopsy findings showed the superior lobe of the right lung a cancerous mass containing many small tuberculous cavities which were almost obliterated by the cancerous ingrowth. Microscopic examination of the lung tissue showed epithelioma. The right pleura and mediastinal and cervical glands showed cancerous involvement and the superior vena cava was compressed by a mass of fibrocarcinomatous tissue. The second case was diagnosed at necropsy. The lung was filled by a caseating mass containing giant cells. Foci of definite malignancy were found in the bronchi. The alveolar spaces were also filled with large deeply stained cells containing prominent nuclei, many of which showed active cell division. Cancer secondary to old tuberculosis is perhaps not rare. The epithelium of the bronchi and alveolar spaces can undergo cell division and become malignant in the same way that the other tissues in the body undergo malignant changes. Letulle states that his two cases of primary cancer and tuberculosis are a much rarer condition than the association of a metastatic cancer and tuberculosis. Metastasis to the lung and pleura, either by emboli or by direct extension is quite common.—*Tuberculose pulmonaire et cancer primitif du poumon. M. Letulle, Presse Méd., August 7, 1920, xxviii, 537.*

Tumor Like Tuberculosis of the Heart.—A postmortem revealed an unusually large conglomerate tubercle in the left auricle. The disease may have had its origin in a tuberculous bronchial lymph node. Another case of chronic myocardial tuberculosis of nodular type is described.—*Tumorartige Tuberkulose des Herzens, A. Binder, (Ztschr. f. Herz-u. Gefässkrankh., 1920, xii, no. 1) Zentralbl. f. innere Med., 1920, xli, 462.*

Tuberculosis of Meckel's Diverticulum.—A case of tuberculosis of Meckel's diverticulum observed at the Pathological Institute at Bonn is described; the disease also involved the serosa with small miliary nodules. Tuberculous involvement of the lungs and intestines was associated.—*Tuberkulose des Meckel'schen Divertikels, T. Wirtz, (Inaug. Diss., Bonn, 1920.), Zentralbl. f. Chir., 1920, xlvii, 933.*

Pulmonary Silicosis.—The article deals with workers engaged in the following industries: manufacture of silica bricks, and silica flour milling, scythe stone-making, lead mining, quarrying, and stone-dressing. Under pathogenesis, air pollution by dust, the essential fineness of dangerous silica dust and the specific qualities of silica as a disease producer are discussed. The gross characters and the microscopic structure of the silicotic lung as well as incineration results are gone into. The symptoms vary in nature and time of onset; among the early ones are dyspnea, cough, and hemoptysis. Five typical instances are then described. After a thorough discussion of the prognosis the following conclusions are drawn: 1. Silicosis is caused by the inhalation of minute particles of dust of high silica content. 2. The finest particles are most directly injurious as they reach the lymphatic channels of the lung producing progressive fibrosis; the dust is most dangerous at the beginning of its generation, before damping or agglutination has occurred. 3. The disease produced can be diagnosed from physical signs—in some cases before the patient has become aware of definite symptoms. 4. Silicosis predisposes to tuberculosis, as a result of the changes produced in the lung. It may, however, exist and prove fatal without any definite evidence of a superadded tuberculous infection. 5. The only means of combating the disease is by prophylaxis—in preventing the generation of dust at its source, in obviating its inhalation by the use of masks, and in excluding any affected persons when the condition becomes recognizable. 6. The prophylactic measures should be carried out in all industries where the inhalation of dust of high silica content is a contingent danger.—*A Study of Pulmonary Silicosis, E. L. Middleton, J. Industr. Hyg., March, 1921, 11, 433.*

Secondary Pulmonary Hypertrophic Osteoarthropathy.—The patient described developed pathologic changes in the extremities as a result of a chronic fibrous pulmonary tuberculosis. He had swelling of the distal extremities of all the limbs, most marked in the legs and feet. The swelling was due to three conditions: (*a*) hyperemia, (*b*) fibrous tissue thickening of the subcutaneous tissue, and (*c*) ossifying periostitis of the long bones. He had (*a*) permanent globular enlargement or clubbing of the distal phalanges of the fingers and toes; (*b*) parrot-beak deformity of the nails of the toes and fingers; (*c*) subperiosteal deposit of bone along the shafts of the long bones of the extremities and (*d*) thickening of the tip of the nose and to a less marked degree of the malar regions. Many of these cases are overlooked because of lack of acquaintance with the definite group of symptoms and pathologic changes. In institutions in which lung lesions, such as bronchiectasis, chronic pleuritis, tuberculosis and abscesses of the lung, are numerous, this disease is seen frequently enough as a complication. In the average private and hospital practice, on the other hand, hypertrophic osteoarthropathy is very uncommon. Yet so characteristic are the evidences of this disease that, once a case is seen, the condition will always be readily recognized. —*Secondary Pulmonary Hypertrophic Osteo-Arthropathy: Report of a Case: S. Kleinberg, J. Am. M. Ass., February 12, 1921, lxxvi, 435.*

Surgical Tuberculosis.—Tuberculosis of the joints and bones should not be considered as purely local lesions. So called surgical tuberculosis is above all a medical disease. In the large majority the surgical tuberculosis is of hematogenous origin. The bacilli enter the mucous membranes and penetrate them without causing a local lesion. This explains the enlargement of the tracheobronchial and mesenteric lymph glands, when the pulmonary mucous membrane and the intestinal mucous membrane are the portals of entry. Cervical adenitis is due to mucocutaneous inoculation about the head. The infection, though often not tuberculous at the outset, may become so later. The enlarged gland in itself is not dangerous, but it is a menace to the organism, because it contains bacilli which at any time may become disseminated through the blood and may localize in the bones or joints. The cause of the setting free of the tubercle bacilli may be an attack of measles with bronchopneumonia, grippe or more rarely, scarlet fever. Tuberculous osteoarthritis may be preceded by pleurisy. This dissemination may be accompanied by fever, because simultaneously with the bacilli, toxins are put in circulation. In infants in whom tuberculosis tends to be generalized, one observes first a cutaneous nodule, later spina ventosa, osteitis of the os calcis, cold abscess of the knee, coxalgia and Pott's disease. While these manifestations do not appear at the same time, the localization of the bacilli occurs in the course of the same dissemination, but the more superficial and accessible the lesion, the sooner does it manifest itself.—*Les tuberculoses chirurgicales en général, A. Broca, Progr. Méd., 1920, lii, 565.*

Brown-Sequard's Syndrome in Pott's Disease.—A woman of forty-five, suffering from suboccipital Pott's disease, felt something crack in her neck while an orderly was placing her head on an X-ray plate. From that moment on, she could not move her head and her left arm and leg were completely paralyzed. On the other hand, neuralgic pains in the neck and face which had been very severe decreased a good deal. The head of the patient is inclined to the right and forward, the chin touching the sternum. In the nape of the neck just under the occiput and principally to the left of the median line, there is a very hard protuberance which makes the impression of a luxation of the atlanto-axoid articulation. The neurological examination reveals the following: 1. On the left a complete flaccid paralysis of the upper and the lower extremity, of the respiratory muscles and of the diaphragm; 2. on the right, a complete anesthesia and analgesia from the foot to the neck, but leaving the trigeminal area intact. This typical Brown-Sequard syndrome lasted only two days, after which time the anesthesia remained limited to the right side while the paralysis affected all four extremities. The patient died. The autopsy showed an atlanto-axoid luxation, more to the left and, on the articular surfaces, granulations mixed with pus. The uppermost portion of the spinal cord showed a linear transverse fissure through its left half as if it had been cut across. The tissue was softened at that level.—*Syndrome de Brown-Séquard au cours d'un mal de Pott sous-occipital, C. Roubier, Progr. Méd., October 2, 1920, no. 40, 435.*

Erythema Nodosum and Tuberculosis.—The case observed and reported by Stokes supplies clinical evidence, though no conclusive proof, for the belief that erythema nodosum may in some cases be of tuberculous origin. The patient, a girl of nineteen years, came to the clinic complaining of an eruption over shins and knees, associated with severe rheumatism of one week's duration. She had been exposed to tuberculous infection. On examination the erythema nodosum failed to show the usual hemorrhagic changes. No focus of septic infection could be found. Under rest in bed and the administration of salicylates the patient improved. Twenty-two days after the first examination she developed symptoms of a fulminating tuberculous meningitis and died seven days later. Tubercle bacilli were found in the spinal fluid. Necropsy disclosed an extensive recent miliary tuberculosis involving all the viscera. The outstanding features of interest in this case are the absence of clinical evidence of tuberculosis when the patient presented herself with rheumatoid symptoms and erythema nodosum, the apparently exact correspondence of the onset of erythema nodosum with the time of generalization of the tuberculous infection, as estimated by the age of the tubercles, found at necropsy, and the complete absence both in life and at necropsy of the septic foci responsible for erythema nodosum of the streptococcal types.—*Erythema Nodosum and Tuberculosis. Report of a Case Terminating in Tuberculous Meningitis, With Necropsy, J. H. Stokes, Arch. Dermat. & Syphilol., January, 1921, iii, 29.*

Feeblemindedness and Tuberculosis.—The study of symptoms of tuberculosis teaches us more than the study of the bacillus of Koch. As bacteriology with all its splendid achievements put such emphasis on the cause, the effects were overlooked. Since feeblemindedness was in no immediate sense a cause of tuberculosis, it was scarcely considered. But in seeking effects of feeblemindedness, tuberculosis cannot be overlooked. Physical diseases generally have psychic effects. Some evidence has been produced that there is a definite group of cases of dementia precox in which tuberculosis may be considered a causative factor and possibly the causative factor. Mental symptoms of less severe nature, however, are far more frequent. Representative of mental diseases stands feeblemindedness. By means of the Binet-Simon test and its modifications, we can measure intelligence defect, and hence we can grade the feebleminded on a certain basis with a considerable degree of accuracy. These are the idiots, the imbeciles, the morons and the subnormals. The numerical frequency of the disease was estimated at from three to twenty per thousand before the war. The data from the draft board examinations disclosed the fact that over 5 per cent of all rejections were because of mental defect. In some states the rejection for feeblemindedness exceeded 10 per cent of all rejections. Many, if not most, of the social evils of the world arise upon a basis of feeblemindedness and among these effects tuberculosis along with syphilis must be to a certain extent definitely included. Squalor and want breed tuberculosis, poverty fosters its spread, feeblemindedness stands back of all these. The feebleminded mother bears feebleminded children, and more abundantly than normal. Crowding, poverty and filth are added. Feeblemindedness starts the prostitute's life; tuberculosis ends it.—*The Relation of Feeblemindedness and Tuberculosis, K. A. Menninger, J. Outdoor Life, September, 1920, xvii, 251.*

Tuberculosis of the Penis.—A case of chronic hyperplastic tuberculosis of the penis is described which was confined to the corpus cavernosum. The focus was entirely encapsulated. The source is supposed to be hematogenous.—*Über Tuberkulose des Penis, H. Thielmann, (Inaug. Diss., Bonn, 1920), Zentrabl. f. Chir., 1920, xlvii, 1026.*

Heminephrectomy of a Horseshoe Kidney for Tuberculosis.—The right half of a horseshoe kidney was found upon operation to be tuberculous with marked disintegration and distinct demarcation between the normal and the diseased side. The urinary findings were typical,—tubercle bacilli with blood and numerous leucocytes. The bladder and ureter on the right side were involved while the left side was normal. The patient died seven weeks after operation.—*Heminephrektomie bei Halbseitentuberkulose einer Hufeisenniere, G. Magnus, Zentrabl. f. Chir., 1920, xlvii, 76.*

THE
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The Abstract Editor is Dr. George Mannheimer, 41 West 51st Street, New York City. Prompt transmission to him of reprints or abstracts of papers on tuberculosis, sanatorium or board of health reports, etc., will promote their early publication in this section.

Abstracts should be sent typewritten on one side of the page only. They should be as concise and compact as the subject matter of the article warrants. They should be headed with a short title, and followed by the full title of the paper, author's name, journal, date, column and page.

The Influence of Smoke Abatement upon Tuberculosis.—It is a well established fact that sunlight is the most potent enemy of the tubercle bacillus. Moreover, it is also well known that the presence of dust or dirt in the air, smoke dust, for example, is detrimental to the sufferer from tuberculosis for obvious reasons. Light is not only destructive to the tubercle bacilli, but invigorates the system and enables one better to withstand the onslaughts of most diseases, and those of bacterial origin in particular. Accordingly, the action of sunlight is twofold and of inestimable value in one way or the other. These facts then bring us to the point, the influence of smoke abatement upon tuberculosis. In the *Sunday Observer* published in London, there is a weekly letter from a medical correspondent. In the issue of January 23, 1921, this correspondent in discussing the evil influence of a smoky atmosphere upon tuberculosis, declares that the principles evolved by Koch have been marvellously applied in New York. That is, by abolishing the smoke nuisance, the New York Board of Health has made of the city a city of light and thus immensely increased the chances for recovery of the tuberculous. The law for the abolition of smoke in New York came into effect in 1905 and it is stated that the results have been almost magical. The figures given in support of this statement are as follows. At about the beginning of the century pulmonary tuberculosis killed thirty-nine per ten thousand per annum in New York: in 1919 it killed thirteen. This signifies that in twenty years or thereabouts, the death rate from this disease has been reduced to one third of its former proportion.

It is argued that if measures for smoke abatement brought about this great change for the better in New York, similar measures would accomplish even more in London, where conditions with regard to smoke and dirt are infinitely worse. Pittsburgh has been cleaned, largely by means of smoke abatement measures, and there seems to be a consensus of opinion that the cleaner the air of a place is, the better it is for people suffering from bronchial and other respiratory affections, and perhaps especially for those afflicted with the pulmonary form of tuberculosis. But that a clear atmosphere is beneficial to health is obvious to all, and no longer should a smoke laden air be permitted in a civilized country. Why not have unpolluted air as well as unpolluted waters? A comparatively pure water supply has resulted almost in the abolition of some epidemic diseases and it is reasonable to suppose that a comparatively pure air might in course of time abolish certain other diseases. In any event, such an air is healthier and more pleasant by far and, moreover, is not very difficult of attainment.—*Editorial article, N. York M. J., April 6, 1921, cxiii, 542.*

Tuberculosis in New York City

Quarters Ending December 31, 1919 and 1920

		MANHATTAN	BRONX	BROOKLYN	QUEENS	RICHMOND	CITY
Population	1919	2,286,550	716,512	2,002,289	457,398	114,414	5,577,163
	1920	2,281,664	747,520	2,042,246	476,224	117,503	5,665,157
New cases	1919	2,103	508	907	239	37	3,794
	1920	1,906	336	1,014	304	54	3,614
Total cases in register	1919	17,449	3,583	7,212	1,525	267	30,036
	1920	15,505	3,490	7,030	1,576	318	27,919
New patients examined at clinic	1919	1,981	442	1,230	156	25	3,834
	1920	1,587	425	1,204	250	27	3,493
Cases under supervision	1919	130	143	368	8	5	654
	1920	182	20	390	19	7	618
Voluntary renovations	1919	386	73	221	97	42	819
	1920	257	86	177	275	26	821
Sputum examined	1919	5,790	1,588	2,766	484	98	10,726
	1920	5,062	1,198	2,375	446	107	9,188
Positive sputum	1919	1,133	314	515	102	14	2,078
	1920	965	166	464	109	24	1,728
Deaths from pulmonary tuberculosis	1919	693	161	453	83	28	1,418
	1920	585	123	448	105	23	1,284
Death rate per 1,000 of population	1919	1.20	0.89	0.99	0.72	0.97	1.01
	1920	1.02	0.65	0.87	0.88	0.78	0.90
Deaths all form of tuberculosis	1919	794	183	518	93	32	1,620
	1920	682	151	500	119	23	1,475
Death rate all forms	1919	1.38	1.01	1.03	0.81	1.11	1.15
	1920	1.19	0.80	0.97	0.99	0.23	1.03

—*Weekly Bull., Dpt. of Health, N. Y. City, April 9, 1921, x, 117.*

The Campaign against Tuberculosis.—Medical officers for the past twenty-five years have urged the case of prevention before that of cure, but governing authorities have not grasped this important fact. Patch-work systems have been preferred. The author stresses the importance of proper housing, demolition of slum areas, creation of open spaces and a pure milk supply. Large amounts are properly spent on child welfare work but a better social environment must also be created. The whole doctrine of public health is prevention.—*Some Observations on the Campaign against Tuberculosis, W. Robinson, Med. Officer, February 5, 1921.*

Statistics on the Prevention of Pulmonary Tuberculosis.—Statistics show that in spite of all that has been said and done for the prevention of tuberculosis, the efforts in regard to pulmonary tuberculosis have not been attended with the anticipated success. The decline in mortality from this cause dates from 1838, and has continued steadily ever since, down to 1913. Koch's discovery of the tubercle bacillus in 1882 does not seem to have affected it in any way. Comparing the average mortality per million living in the first six years of the period 1902 to 1913 with the last six years, in the air borne diseases, the following result is found: Pneumonia shows a decline of 14 per cent, phthisis of 11.6 per cent, bronchitis of 10.68 per cent, and the four zymotic diseases (measles, scarlet fever, whooping cough, diphtheria) of 21 per cent. All these diseases are closely associated. The common cold is probably the most important connecting link between all respiratory infections. It is the means of disseminating air borne disease and of preparing the soil for further invasions or for the condition of carrier. The campaign against tuberculosis must be directed against the air borne diseases as a whole, and against the common cold in particular.—*Some Deductions from the Statistics on the Prevention of Pulmonary Tuberculosis, D. H. C. Given, Brit. M. J., February 12, 1921, 225.*

Courses in Tuberculosis.—Throughout the year the Ohio State Sanatorium will conduct short courses of ten days each, available to all physicians of Ohio without cost. The school is organized with confidence that opportunity for further knowedge of the diagnosis of chest diseases is imperatively needed and with optimism that the physicians will avail themselves of the facilities peculiarly accessible at the State Sanatorium. It is well known that the good diagnostician of tuberculosis is also a good diagnostician of the other common chest conditions. A large inspiration has been derived from the plea of the National Tuberculosis Association for the establishment of special medical courses. Such are held to be outstanding needs in the white plague campaign. It is hoped to blaze a trail in this work whereby other sanatoria similarly situated may perhaps follow, to fill the nation-wide need for better trained chest diagnosticians in general practice. This opportunity to review the intricate and finely balanced details of chest examination is believed highly valuable to every physician and is sure to bear fruit in more accurate physical examinations subsequent to attendance during the session of one of these courses. The courses offered by the United States Public Health Service at its various district headquarters (but restricted to ex-service physicians) have demonstrated their value and popularity by the numerous requests that have been made to open the courses to all physicians without restriction. We believe there is a general awakening as to the need of better training in the fight against tuberculosis. As one step in providing this training, the facilities for clinical and diagnostic instruction at the Ohio State Sanatorium are herewith made available for the physicians of Ohio.—*Pamphlet, issued by the Ohio State Sanatorium, Mount Vernon, O., School of Tuberculosis.*

Giant Cell Formation.—Sections of tubercles from rabbit's lungs reveal the development of giant cells from the vascular endothelium. Sections from actinomycosis of cow's tongue reveal giant cells in vascular granulation tissue.—*Beitrag zur Riesenzellenfrage, L. Cost, Dissertation, Giessen, 1919, translated from Internat. Centralbl. f. d. ges. Tuberk. Forsch., 1920, xiv, 16.*

Squint, Lefthandedness and Tuberculosis.—In a book by the author it was claimed that squint was about three times more common in consumptives, and probably also in consumptives' parents, than in the nontuberculous; that such squint seemed to favor the left eye; and that tuberculous squinters were lefthanded and gave a family history of lefthandedness, oftener than did nonsquinters. These five points are examined further on a larger material with the following results: Ordinary concomitant strabismus in 500 adults or adolescent consumptives (all sputum positive) 1.2 per cent; in comparable controls only 0.4 per cent. Of 343 cases of juvenile phthisis examined in Yorkshire, there were 11 squinters or 3.2 per cent. Bishop Hannan's recent London figures with ordinary school children revealed 1.5 per cent of squinters. The conclusion is reached that in the subjects of some forms of tuberculosis squint is twice or three times as frequent as in normal persons. Squint is excessive in lung and lymph gland tuberculosis, but not in bone or joint tuberculosis. Squint is excessive among the clinically nontuberculous mothers of nonsquinting consumptives. Of 65 phthisical squinters, 48 squinted with the left eye. Of 62 nontuberculous squinters 40 were left sided. It appears likely that left eyed preference is a characteristic of squint generally. Lefthandedness or mancinism occurs in 2 to 4 per cent of the general population. Rivers found it in 2.7 per cent of nonsquinting consumptives. In 60 squinters it occurred four times (6.6 per cent). Whether in phthisical or in nontuberculous subjects, left eyed concomitant strabismus is somewhat associated with mancinism, and with a family history of mancinism. To say that tuberculosis causes the squint is inadmissible because the history was always of the squint coming first; also there were signs of phlyctenules in very few of these patients. There is a distinct suggestion of the development of clinical tuberculosis being favored by an abnormal constitution of which squint is a sign.—*Squint, Mancinism and Tubercle, W. C. Rivers, Lancet, February 12, 1921, cc, 319.*

Types of Pulmonary Tuberculosis under the X-Rays.—1. Pulmonary tuberculosis can be divided into clinical and nonclinical types with a high degree of accuracy by sterescopic plates. 2. Unless we make this division into the two types we are putting our method on the level of tuberculin which will not differentiate between infection with the tubercle bacillus and the disease tuberculosis. 3. Negative stereoscopic plates can with an occasional rare exception exclude a clinical type of tuberculosis. 4. Parenchymatous tuberculosis is a clinical type unless slight in amount and definitely calcified, and peribronchial tuberculosis is of clinical significance only where it conforms to the following qualifications: upper or middle lobe distribution, unilateral or more marked on one side as compared with the opposite, gross in amount and presenting a hazy outline with definite modulations. 5. A negative diagnosis from the roentgenologist if of more value than a positive, in that in the face of suggestive symptoms, a positive diagnosis can often be made by other methods, but the X-ray alone offers the only accurate method of excluding the disease.—*The Clinical Importance of the Different Types of Pulmonary Tuberculosis as Determined by Roentgen Examination, R. G. Allison, Am. J. Roentgenol., March, 1921, viii, 103.*

Diagnosis of Pulmonary Tuberculosis.—Of 158 cases observed in the Brompton and Victoria Park chest hospitals, no less than 124 or over 78 per cent were reported as not suffering from tuberculosis; while of the 34 cases held to be tuberculous, 10 were looked upon as arrested and not requiring active treatment. In all, therefore, 24 cases only or 15 per cent of the 158 observed were recommended for treatment. The difference of opinion in respect of many cases that existed on the one hand between the Ministry of Pensions Boards and the tuberculosis officers, and on the other hand between the tuberculosis officers and the staffs of the chest hospitals, was not helpful to the official tuberculosis administration. The records taken collectively illustrate the difficulties in connection with the diagnosis of tuberculosis. To a lay committee it must be surprising that upon such an important issue as the presence of tuberculous disease there is room for so much disagreement by experts. Unfortunately, when there is a division of opinion, there is no means of determining on which side the truth lies. As to this, however, the after-histories of the cases concerned, will, in time, give some clue. As yet, in two cases only has a case reported by a hospital as being not tuberculous shown conclusive evidence of the disease at a later date. On the other hand, in one instance a case recommended by a tuberculosis officer for diagnostic observation was within fourteen days admitted to a home for very advanced cases. An important practical point which arises is the question of disposal and treatment of cases concerning whose condition there is a conflict of expert opinion. Some authorities urge that the doubtful and suspected cases, more than any other class of patient, are those for whom sanatorium treatment is most clearly indicated. Others, whose opinion carries no less weight, contend that such cases need nothing more than advice and periodic supervision, and that to label them as tuberculous by sending them to a sanatorium is to do the patient a great disservice. In London, the practice is elastic in this respect, the circumstances of individual cases determining the recommendation as to disposal. One principle, however, is followed constantly, namely, that all cases which have passed through an "observation" bed, irrespective of the expert findings, are referred to the appropriate tuberculosis officers and medical practitioners for such subsequent supervision as may be thought necessary. A copy of the report received from the observing hospital is, at the same time, forwarded to the tuberculosis officer and to the patient's usual medical attendant.—*The Diagnosis of Pulmonary Tuberculosis, N. Bardswell, Tubercle, March,* 1921, *ii, 257.*

Diagnostic Value of X-Ray Examination.—Since the earliest days of roentgenology the aid of the X-ray examination has been invoked for diagnostic assistance in cases of suspected pulmonary tuberculosis and to-day its employment is a very important part of the routine examination of the chest. Nevertheless, there is considerable confusion concerning the interpretation of the shadows seen on the plate. The X-ray appearances of pulmonary tuberculosis vary with the stage of the disease. The shadow cast by the pathological tissues may be of any degree of density, including the faint filmy shadow of the very early case, the mottling of the more advanced disease and the dense shadow of the healed lesion. At times, the first indications of disease will be detected by the physical examination; at other times the X-ray alone will show the early changes and the X-ray affords the most accurate information that can be obtained apart from the autopsy, at least for the extent of the disease. Usually when physical signs are present, the X-ray will demonstrate the area of involvement to be more extensive than was indicated by the physical examination. No method or combination of methods at present employed will detect invariably the earliest signs of disease in every case nor decide positively at all times the activity of a lesion. The X-ray will demonstrate the site and the extent of the tissue changes, and although usually it is possible to infer from the plate alone whether the lesion is active or not, this decision should be left to the clinician to make. To discover on the plate indications of pathological changes in the tissues, usually requires the support of clinical evidence of disease, before concluding that the changes can be due only to tuberculosis. Otherwise the discovery may consist of nothing more than the recognition of a condition which has long since ceased to be a matter of medical interest. The clinical support need not be confined to the presence of physical signs within the chest, but may be manifested by the presence of general symptoms of ill health. Definite indications of pathological changes in the lungs so often are seen on the X-ray plate, not only in individuals who apparently are in perfect health, but also in those who give no history of having suffered from a serious illness at any time, that one is forced to the conclusion that tuberculosis of the lungs is frequently a mild disease, often running its course from onset to recovery unrecognized. —*The Diagnostic Value of the X-Ray Examination in Pulmonary Tuberculosis, W. A. Wilkins, Canad. M. Ass. J., November, 1920, x, 99.*

Glandular and Pulmonary Tuberculosis.—A constant fact, observed in fifty years experience, is that the members of families with an inherited predisposition to the disease who suffer from cervical gland lesion leading to suppuration do not contract pulmonary tuberculosis or any other form of the malady, whereas several other members of the same families without gland lesion, and often the more robust individuals, frequently develop consumption. The conclusion to be drawn is that the absorption of tubercle bacilli from the surface of the mouth when conveyed by the lymphatic vessels and arrested in the glands, as indicated by these glands breaking down, leads to the production there of a type of bacillus capable of curing consumption, and conferring immunity without the bacilli themselves going beyond the gland.—*Glandular and Pulmonary Tuberculosis, W. Williams, Brit. M. J., January 29, 1921,* 158.

Diagnosis and Significance of Tracheobronchial Adenopathy.—Conclusions: 1. A positive D'Espine sign is indicative of enlarged glands at the root of the lungs. 2. Enlarged tracheobronchial glands may be due to any one of several causes, the chief of which is an infection by the tubercle bacillus. 3. If tonsilitis, whooping cough or measles causes enlarged tracheobronchial glands, they are usually not of sufficient size or density to give a positive D'Espine sign. 4. Chronic bronchitis will produce enlarged tracheobronchial glands which can be differentiated from a tuberculous hilum by means of the roentgenogram. 5. A positive D'Espine sign found in a poorly nourished child usually is evidence of a tuberculous infection of the hilum. 6. The degree of the infection can be determined by the roentgenogram. 7. Weight below standard is very common in children with a chronic tuberculous infection. 8. A child with a massive chronic tuberculous infection is a candidate for active tuberculosis, and should be watched carefully for early signs and symptoms. 9. In chronic tuberculous infections in children, few signs can be elicited by physical examination. 10. The degree of the infection in childhood is an important factor in determining whether or not a child will develop active tuberculosis in adult life. 11. Every child should have a thorough physical examination with the idea of determining if possible whether or not there is a tuberculous infection of the chest, and if so, how heavy. 12. Those with evidence of massive infections should be taught how to live and should be instructed in the signs and symptoms of early tuberculous activity. If this were done, the number of advanced cases of pulmonary tuberculosis would be greatly reduced.—*Diagnosis and Significance of Tracheobronchial Adenopathy, R. M. Balyeat, J. Am. M. Ass., April 9, 1921, lxxvi, 988.*

Tuberculous Hemarthrosis of the Knee.—Only a few cases of this condition are on record. The patient, a girl of fifteen, was admitted to the hospital suffering from multiple tuberculous lesions. The glands of the neck were involved; there were small lesions in connection with the epiphyses of the left wrist, right ankle and right elbow and a tuberculous dactylitis. There was no history or evidence of hemophilia. The right knee had been swollen and painful from the time of admission. At first the application of extension to the knee relieved the pain, but the swelling became more marked. Gradually the swelling became extreme and the pain severe. Exploratory puncture revealed a large quantity of dark fluid blood and a few clots. After the evacuation of the blood, improvement continued for ten days when the joint became rapidly distended and a further quantity of blood was evacuated. A third bleeding occurred a week later; the blood was evacuated, after which there was no further hemorrhage. The patient's health improved; the joint remained slightly swollen and tender and the synovial membrane distinctly pulpy.—*Tuberculous Hemarthrosis of the Knee, J. A. C. Macewen, Brit. M. J., January 29, 1921, 158.*

Tuberculous Lymphangitis.—Two cases of superficial lymphangitis are reported. The one involved the entire arm like a chain of beads outlining the course of the lymphatics. It arose from a primary lesion on the thumb, resulting from an abrasion infected from a fistulous testicular tuberculosis. The other also involved the arm up to the axilla, starting from an ulcer on the left index finger in an advanced case of intestinal and peritoneal tuberculosis. The clinical picture is that of a slow painless development of more or less firm nodules along an indurated lymph path. The nodules can soften and rupture. The prognosis is that of the general disease.—*Über tuberkulose Lymphangitis, B. Kipris, Dissertation, Berlin, 1918, translated from Internat. Centralbl. f. d. ges. Tuberk. Forsch., 1920, xiv, 121.*

Chronic Tuberculosis of the Kidney.—Chronic infection of the kidney as a primary lesion in the body does not exist. Unilateral chronic renal tuberculosis results from a previously existing focus elsewhere in the body by way of the blood stream. The bladder involvement is secondary. The disease usually manifests itself as a chronic pyuria. Every positively diagnosed case of unilateral renal tuberculosis must be operated.—*Beitrag zur Frage der chronischen Nierentuberkulose, J. Diener. Dissertation, Kiel, 1919, translated from Internatl. Centralbl. f. d. ges. Tuberk. Forsch., 1920, xiv, 122.*

Tuberculosis of the Kidney in Women. The following conclusions are formulated from an experience with 77 cases. 1. In cases of renal tuberculosis, in 18 per cent there has been a family history of tuberculosis. 2. In 60 per cent of the cases of tuberculosis of the urinary tract the lesion has been in the right kidney, in 35 per cent in the left kidney, and has been bilateral in four patients. 3. Renal tuberculosis occurs most frequently between the ages of twenty and forty, 71 per cent. 4. The average duration of symptoms before coming to the hospital was thirty-three months. 5. Renal tuberculosis in colored women, although not as frequent as in white, is by no means rare. 6. In 88 per cent of cases dysuria and polyuria were the first symptoms. 7. One-third of the women complained of hematuria on admission, and in eight patients smoky urine was the first symptom. 8. Thickening and tenderness of the portion of the ureter palpable on vaginal examination was present in 32 per cent of the patients, and this sign is of great help in the early detection of cases of renal tuberculosis. 9. Of the seven patients not operated on, four are known to be dead and the other three left the hospital in a very bad condition and are probably now dead, although there is no definite information about them. 10. The 3 women on whom simple nephrotomies were performed all did badly. 11. The ultimate result is known in 42 out of 67 cases in which the kidney was removed, or in 62 per cent of the cases. 12. Seven of these 42 patients may be classed as greatly improved and are now alive, six years after their operations; 25 are entirely well with an average period of eleven years since they were discharged from the hospital. This means that 16.5 per cent of the women of whom there is record have been greatly improved by their operations and 59.5 per cent have been entirely cured. 13. Comparison of the results obtained when the ureter is removed with the kidney and when it is left *in situ* shows that, although the ultimate results are the same following the two methods, the postoperative sinus heals more rapidly when a nephro-ureterectomy is done, and this therefore, seems to be the operation of choice when the patient's condition warrants a prolongation of the anesthetic.—*Tuberculosis of the Kidney in Women, L. Brady, Bull. Johns Hopkins Hosp., January, 1921, xxxii, 13.*

Tuberculous Salpingitis.—The findings of 200 cases of tuberculous salpingitis are summarized as follows: 1. Tuberculous salpingitis occurred in nearly 1 per cent of all women admitted on the gynecological service of the Johns Hopkins Hospital. 2. It was found one and a half times as frequently among the colored women as among the white. 3. Out of every 13 abnormal tubes removed at operation, one was tuberculous. 4. Nearly three-fourths of the patients were between twenty and forty years of age. 5. Sixty per cent of the married patients were sterile. 6. A family history of tuberculosis was reported in 22.5 per cent, while in an additional 2.5 per cent the consort had active pulmonary tuberculosis. 7. The chief complaint of the patient was pain (74.5 per cent) usually situated in the lower abdomen (82.5 per cent). 8. Not much information was obtained from the menstrual history. However, 62 per cent of the patients had dysmenorrhea and 41.5 per cent menorrhagia. Amenorrhea occurred in only 6.5 per cent of the patients. 9. Leucorrhea occurred in 72 per cent of the patients. 10. Nearly half of the patients had dysuria, nycturia and pollakiuria. 11. More than half of the patients were constipated. 12. Approximately one-fourth of the patients attributed the onset of their symptoms to some uterine activity (menstruation, pregnancy, etc.). 13. Half of the patients had lost weight during their illiness. 14. The physical examination presented no characteristic findings. 15. About one-fourth of the patients had pulmonary tuberculosis. 16. Pre-operative elevation of temperature was recorded in 62.5 per cent. 17. There was usually either an absolute or a relative leucopenia. 18. Half of the patients examined had a hemoglobin below normal limits. 19. The correct diagnosis before operation was made in only 13 per cent of the cases and in more than half of these the diagnosis was aided by the presence of ascites. 20. A radical operation was performed in 53 per cent of the cases. 21. Complications during operation occurred in 14.5 per cent of the patients. 22. One hundred and four cases were drained. Of these, 17.3 per cent developed fecal fistulae. Abdominal fecal fistulae occurred 3 times more frequently among the cases drained abdominally than in those drained through the vagina. 23. In one-third of all the patients, there was suppuration of the abdominal incision. 24. No patients who were not drained, developed a fecal fistula. 25. The incidence of fecal fistulae among the cases in which the bowel had been injured was 48 per cent, whereas among the cases in which the intestines had remained intact, the incidence was only 3.4 per cent. The patients with pre-operative fever developed fecal fistulae more than twice as frequently as those without fever. 26. Urinary fistulae occurred 5 times (2.5 per cent). 27. The order of frequency of involvement of the pelvic organs was as follows: tubes, uterus, ovaries, cervix and and vagina. Tuberculosis of these organs was found associated with tubal tuberculosis as follows: uterus, 72.6 per cent; ovaries, 33.1 per cent; cervix, 3.5 per cent; and vagina, 0.5 per cent. 28. In 99 per cent of the cases both tubes were involved. 29. In 68 per cent of the cases the peritoneum was involved, and in 3 per cent the appendix was tuberculous. 30. In 17 per cent myomata uteri were associated with the tuberculous process. 31. In only 2 per cent was there an associated involvement of the urinary tract. 32. The prognosis is grave in the presence of tuberculosis elsewhere in the body, where fever exists and where the peritoneum is involved. 33. The operative mortality was 7.6 per cent. (This includes all the patients who died in the hospital.) 34. By means of follow-up letters, etc., 90 patients were traced and out of this number, 78 were found to be living from 2 months to 30 years after the operations. Nearly all those who are alive are in good condition.—*A Clinical Study of Tuberculous Salpingitis, based upon 200 Cases, J. P. Greenberg, Bull., Johns Hopkins Hosp., February, 1921, xxxii, 52.*

Tuberculous Meningitis.—Eighty cases of tuberculous meningitis seen by the author have followed grippe or have appeared a short time after it, grippe having been the cause only occasionally. One patient had had pneumonia a month before. Meningitis appeared suddenly and death occurred within forty-eight hours. Another patient convalescing from pneumonia was taken ill suddenly within a week, and twelve hours later he was dead. At the necropsy suppuration of the meninges was found. The pus contained only the pneumococcus. In two cases the meningococcus was associated with the pneumococcus. In some cases only the streptococcus was present. In the tuberculous cases, the tubercle bacillus was found in 80 per cent of the cases. The mortality in these cases was 100 per cent.—*Acute Meningitis and Tuberculous Meningitis, L. Morquio, J. Ment. & Nerv. Dis., January, 1921, liii, 1.*

Mixed Infection in Surgical Tuberculosis.—Of 80 cases of surgical tuberculosis radical operation under strict asepsis was performed on 22 while 58 were punctured. Thirty-nine had X-ray treatment. Of 71 cases with open foci, 51 perforated spontaneously. Of these 4 were untreated and negative for mixed infection while 47 received ambulatory treatment. Of these 21 were positive for mixed infection and 26 negative; the 20 remaining cases had incisions and fistulas and of these 18 had mixed infections. A large percentage showed a progressive course. Of 9 cases with multiple foci, only one closed, had no mixed infection and had a chronic benign course. The majority of the remainder had mixed infection and a progressive course. The bacteriological findings revealed in 37 staphylococcus pyogenes aureus, in 14 streptococcus pyogenes, in 2 streptococcus and staphylococcus, in 3 xerosis-like bacilli and in 1 bacillus fusiformis. Surgical procedures should be performed under the strictest asepsis. In mixed infection drainage of the pus is necessary. The roentgen ray can be used as a conservative measure and may be of some prophylactic value. The quartz lamp is only valuable in superficial lesions. Orthopedic procedures are difficult in secondary infections, as frequent changes of splints are necessary. Specific therapy fails in the presence of secondary infection. Rollier's sun treatment has given the best results.—*Die Bedeutung der Mischinfektion bei chirurgischer Tuberkulose, M. Jerusalem, Wien. klin. Wchnschr., 1920, 33, 471.*

Pulmonary Sequellae of Influenza.—In many patients attacked by acute epidemic influenza certain sequellae are left in the respiratory tract after the acute disease has run its course. A large number remain with subacute rhinopharyngitis, some with general bronchitis, and now and then there are patients in whom the residual lesion is a localized bronchitis. When the latter affects an upper lobe it is very difficult to differentiate from pulmonary tuberculosis. When these sequellae are instrumental in keeping the patient weak and debilitated for weeks and months, which is often the case, this, in addition to the cough and expectoration, may lead to a diagnosis of pulmonary tuberculosis. More serious pulmonary lesions are bronchiectasis and lung abscess, which have increased in frequency since the last pandemic of influenza. Bronchiectasis remains in cases in which influenza was complicated by pneumonia or pleurisy or both. The diagnosis is at times very difficult, mainly because of the ancient notion that influenza is a strong predisposing factor to tuberculosis. When the lesion is found strictly localized in one of the lower lobes and this is the case in the majority, tuberculosis should be excluded for this reason alone. In those in whom the lesion is in an upper lobe, only repeated sputum examinations decide, though it should count against tuberculosis that the disease began with influenza, that emaciation is not pronounced, that fever is lacking, that the pulse rate is normal, and that there is obtained clear resonance above the clavicle. Where pulmonary abscess remains after influenza, the diagnosis may be made along the same line as in bronchiectasis. In addition note should be made of the fact that the sputum is abundant, at times fetid, the fever continuous or undulating, and pain in the chest is complained of. If several examinations of the sputum fail to disclose tubercle bacilli the diagnosis may be safely made. Leucocytosis with an increased proportion of polynuclear cells points to abscess.—*Pulmonary Sequels of Influenza, M. Fishberg, Am. J. M. Sc., March, 1921, clxi, 365.*

Standardization of Tuberculin.—The chief uses of tuberculin at present are the testing of cattle for tuberculosis, the diagnosis of tuberculosis in man and the treatment of tuberculosis in man. In this paper the test is described as applied in the Wellcome Physiological Research Laboratories. The main test consists in the comparison of a sample with a standard tuberculin. The Pirquet and intracutaneous tests can be used for the standardization of tuberculin. The results obtained by the subcutaneous test have always had to be checked. In all cases where the skin tests are used alone, a control and the standard must be included on the same animal as the samples under experiment. Since August, 1919, 13 different lots of animals have been infected with a constant dose of the same culture. Of these animals, 91 have received doses of standard tuberculin ranging from 1.0 cc. to 0.025 cc. In only two cases were irregular results produced with animals of the same lot. The following factors must be controlled if accurate results are to be obtained: (1) the same strain of tubercle bacilli must be used for infecting the animals; (2) the guinea pigs should be about the same size; (3) all animals to be given tuberculin should be examined and any sick ones discarded; no animals should be used unless the inguinal glands are palpable; (4) the Pirquet test should be used to guide the dosage for subcutaneous injection. The results show that tuberculins can be tested with a reasonable degree of constancy.—*The Standardization of Tuberculin, A. J. Eagleton, Lancet, February 26, 1921, cc, 429.*

Action of Prolonged Pasteurization on Tubercle Bacilli in Milk.—The milk is kept at 60° to 64°C. by steam heated cylinders for twenty to thirty minutes with constant stirring. This procedure had no influence upon the taste, the separation or the albumin or soluble lime salt (phosphate) content. Only amylase of the original milk enzymes is destroyed, while peroxidase and aldehydreductase remain intact. The majority of the lactic acid bacilli are killed. The experiments were performed under practical circumstances. Tubercle bacilli from lesions of the udder were killed, even if pasteurization was only carried out for ten minutes at 60°C.—*Einwirkung der Dauer-Pasteurisierung auf die Tuberkelbazillen der Milch, C. Barthel and O. Stenstrom, Ztschr. f. Gärungsphysiol., translated from Centrabl. f. Bakt. u. Parisitk., Ref., 1920, lxix, 228.*

Mustard Gas and Experimental Tuberculosis.—Mustard gas dissolved in 25 per cent glycerol is bactericidal for virulent human tubercle bacilli after an exposure in vitro of at least one-half hour to 0.1 per cent and after 2 hours to 0.01 per cent. Avirulent human and bovine tubercle bacilli seem to be slightly less sensitive, these organisms requiring an exposure of from 4 hours to one day to obtain the same results. What part, if any, the hydrolysis of mustard gas in the glycerol played in this experiment was not determined. Mustard gas in 0.25 per cent glycerol, containing virulent human tubercle bacilli and injected immediately subcutaneously into guinea pigs, entirely prevented the development of systemic tuberculosis in these animals. Even 0.01 per cent mustard gas has a distinct retarding influence on the development of tuberculosis in these animals. This action could not be due to the tissue-destroying action of the mustard gas in these concentrations, since the same results were obtained in the absence of ulcers. Mustard gas given subcutaneously to guinea pigs in amounts consistent with life (0.001 cc. in glycerol) in a single injection or repeated at four day intervals, for three or four injections, has no appreciable effect on the amount of anatomic tuberculosis resulting from the subcutaneous injections of virulent human tubercle bacilli.—*The Effect of Mustard Gas (Dichlorethylsulphid) on Experimental Tuberculosis, H. J. Corper and O. B. Rensch, J. Infect. Dis., March, 1921, xxviii, 286.*

Leucocytic Response in Experimental Tuberculous Infections.—Guinea pigs have been rendered relatively immune against infection with virulent tubercle bacilli by preliminary inoculation with a suitable quantitity of avirulent tubercle bacilli. Blood counts on these animals show that associated with the immune reaction there is a definite leucocytic response, characterized by an absolute increase in the total count, with an absolute and relative increase in the lymphocytes. The period of greatest activity coincides with that known to be the period of greatest reaction based on anatomical evidence during the course of the infection following this method of immunization. Moreover, blood counts made on animals inoculated with avirulent tubercle bacilli alone show an increase in the circulating lymphocytes during the period of greatest reaction to the infection, while blood counts on guinea pigs inoculated with virulent bacilli alone show an erratic course in which the polymorphonuclear forms are much increased, though not regularly so. These results indicate a parallelism between lymphoid activity and resistance of the animals to tuberculous infection and suggest an association of lymphocytes with the factors determining this resistance, a relation which warrants consideration of the blood picture in the clinical study of tuberculous infection.—*General Leucocytic Response of the Guinea Pig During the Reaction of Artificial Immunity in Experimental Tuberculous Infection, R. G. Hussey, J. Exper. Med., March, 1921, xxxiii, 337.*

Sun Treatment—Of all infectious diseases tuberculosis is the one in which the resistance of the invaded organism plays the most important part in the cure. Surgical tuberculosis is not merely a local disease as formerly believed, but also a general disease demanding general treatment as well as local. Heliotherapy at a high altitude best meets all indications. It is the ideal treatment, since the sun combined with pure mountain air has the desired effect by raising the vitality of the organism and restoring the wasted tissues. Locally, the sun's action is powerfully analgesic and bactericidal, besides reducing inflammation and promoting cicatrization. An experience of seventeen years has proved that sunlight can cure all forms of surgical tuberculosis in all stages and at all ages. By the simultaneous development of the muscles, heliotherapy returns lost beauty to the outlines of the body. It enables us to return to normal life individuals well prepared for work and not maimed and crippled portions of humanity incapable of earning their living. In 1903 Rollier was responsible for the opening of the first clinic in Switzerland for the exclusive treatment of surgical tuberculosis. This establishment of fifty beds soon became insufficient and thirty new clinics have since been added. At the present time there are a thousand beds available for the treatment of surgical tuberculosis. Rollier believes, if heliotherapy can cure tuberculosis, it can also prevent its inception. By founding the *Ecole au soleil des noisetiers* at Cergrat in 1910 he was the first to put into practice this preventive action of the sun. This establishment has two purposes—to save from tuberculosis weakly and predisposed children, and to form an intermediate stage where the convalescents can gradually be prepared for their return to normal life. The results obtained by this school have been so conclusive that one can safely advocate the widespread establishment of similar preventive schools—*The Sun Treatment of Surgical Tuberculosis, A. Rollier, Brit. J. Tuberc., January, 1921, xv, 10.*

X-Ray Treatment of Tuberculous Lymph Nodes.—There are at least five alternative methods of treatment at our disposal for tuberculous lymph nodes: (1) climatic and dietetic, (2) medicinal, (3) tuberculin, (4) surgical, (5) radiation. The paper deals with the last named method, but the others are briefly passed in review. Climatic and dietetic treatment is in the majority of cases inadequate alone, but may be combined with any of the other methods to accelerate recovery. Medicinal and tuberculin treatment accomplishes a cure in about 25 per cent of the cases, according to Rendle Short in his index of prognosis. Surgical intervention is usually instituted in the severest cases. Statistics vary greatly as to the frequency of local recurrences. The best figures are those of the Mayo Clinic, which give a local recurrence rate of 8.6 per cent. Although no definite conclusions can be drawn from published statistics, it seems that X-ray treatment efficiently applied will show results superior to those quoted above. At the same time the usual hygienic-dietetic regimen must not be neglected. There are no contraindications to X-ray therapy. In some cases it may be necessary to combine operative measures with radiation. The size and frequency of the dose can only be determined for each case individually. Generally speaking, we may give large doses at intervals of about three weeks, or smaller doses at shorter intervals. Some cases do better on one method and some on another. It is not contended that X-rays are invariably successful, but a large proportion of cases derive considerable benefit and many are entirely cured.—*X-Ray Treatment of Tuberculous Glands, M. Berry, Brit. J. Tuberc., January, 1921, xv, 13.*

Public Tuberculosis Service—Tuberculosis dispensaries have not as yet taken their proper place. There are many patients who come to the dispensary unnecessarily. It thus becomes overloaded with patients and the tuberculosis officer is unable to devote sufficient time to examination and diagnosis of each individual case and defers them for observation from week to week. Adequate staffing of dispensaries is essential. It will generally be found that a dispensary nurse is only able to do two hours visiting per diem as the rest of her time is devoted to attendance on patients at the dispensary. On this basis a nurse can cope with only 300 to 350 patients. Too little importance has also been attached to preventive work and to efficient care and aftercare of patients. The latter must consist largely in providing suitable work and suitable hours. The gap which now exists between the discharge from a sanatorium and the return to full work is one which is undoing half the work accomplished by these institutions.—*The Organization and Administration of a Public Tuberculosis Service, F. J. C. Blackmore, Brit. J. Tuberc., January, 1921, xv, 20.*

The Influence of Chaulmoogra Oil on the Tubercle Bacillus.—Undiluted chaulmoogra oil and dilutions in paraffin oil had no appreciable germicidal influence in vitro on a strain of bovine tubercle bacilli in the authors' experiments. The sodium salts of the total acids of this oil were not included in this study. Undiluted and diluted chaulmoogra oil had no appreciable germicidal effect on virulent tubercle bacilli by an in vitro-vivo method with guinea pigs. Chaulmoogra oil, in doses of 0.2 cc., per 100 gm. of body weight administered by intramuscular injection at weekly intervals had none or but slight effect on the course of tuberculosis in guinea pigs. Chaulmoogra oil is relatively nontoxic for guinea pigs. Animals have borne at least 11 intramuscular injections of 0.2 cc. per 100 gm. without deleterious effect, except localized inflammatory changes at the sites of the infection.—*The Influence of Chaulmoogra Oil on the Tubercle Bacillus, J. A. Kolmer L. C. Davis and R. Jager, J. Infect. Dis., March, 1921, xxviii, 265.*

Vaccine Treatment of Tuberculosis.—The Dávila vaccine is prepared from tubercle bacilli, wholly disintegrated and emulsified in a perfectly sterilized greasy medium. It includes the bacillary stroma, all the adipocerous material and the free toxins. The bacillary poisons are so attenuated that it has been possible to inject, at once, up to 32 mgm. of this vaccine, without inducing feverish, congestive or any other kind of harmful reaction. Dávila claims that his vaccine contains all the bacillary elements and toxins and that the immunity obtained is therefore complete, whereas the tuberculins necessarily give only partial results. That the vaccine is not inert is proved by the fact that a cutaneous tuberculin test which had been positive prior to the administration of the vaccine, reappears after it. Dávila has proved the efficacy and the relative immediate innocuousness of high doses by experiments on rabbits and other animals. The vaccine employed by the authors was prepared two years ago and has kept without alteration and without losing its activity. Nineteen cases were treated at the sanatorium *La Esperanza* and thirteen at the dispensary. The most remarkable results have been obtained at both places, but at the sanatorium the results were more rapid. Not only incipient but also moderately advanced and even a few far advanced cases were selected. The usual hygienic-dietetic regimen must not be neglected. The treatment should be continued several months after signs of activity have disappeared. The vaccine is employed in the following manner: Two hypodermic injections a week are given in the deltoid region, at first 1 cc. of an emulsion containing 2 mgm. of active substance. The subsequent dose is always double the previous one until 32 mgm. are reached. If the temperature rises above normal, weaker doses are resumed and more gradually increased. Some patients have steadily gained in weight after they have been discharged and returned to their usual occupations. At the dispensary, two pregnant women received the treatment, gave birth to normal children and remained well. The authors recommend the treatment officially to the Department of Sanitation and Charity: 32 cases are reported in detail.—*Treatment of Tuberculosis in Human Beings by Means of the Vaccine Prepared by Dávila, F. Rensoli and S. Fuentes, Sanidad y Beneficienca, March, 1920, xxiii*, 31.

Tuberculinization of Babies.—In our endeavor to abolish pulmonary tuberculosis we fail to identify the unfit, those who are vulnerable to the destructive effects of the tubercle bacillus, and we fail to make ourselves acquainted with the early stage of the disease. Babies suffer from temporary febrile attacks, which seem to be of idiopathic origin and are in no way distinguishable from general reactions induced by tuberculin in those known to be tuberculous; nor are idiopathic pulmonary inflammations distinguishable from focal reactions. Nutritional disorders of babies are not easily distinguished from those of older subjects, afterwards known to be tuberculous. Unsuspected appearances of tuberculosis render it certain that there are many unsuspected carriers. To render these carriers innocuous would entail placing a very large percentage of the population under observation. A testing census of the population is as practicable as revaccinating a whole people against smallpox. It would be of immense value for identifying the unfit, and for rendering timely aid to those whose resisting powers were commencing to wane. Four cases are reported to show that infants under one year may be infected, and that tuberculin can restore them to health while they remain with the source of infection. In order to make the use of tuberculin practicable, reliance should be placed on the skin reaction. Where this is positive, graduated injections of tuberculin should be given until a reaction fails, but in all cases a record of the weight should be kept as an index of the tuberculin effects. The method is simple, safe and free from any remote danger. O. T. is diluted by the tenths method of dilution so that the sixth dilution represents one in one-millionth. A 1 cc. hypodermic syringe, graduated in ten divisions, is used. The fluid is placed just beneath the skin and induration is looked for on the second, third or fourth day. The author suggests one-fifth of one-millionth of 1 cc. for an infant of three months. Most tuberculous babies show a rise of temperature of about 2 degrees during the first six hours succeeding the injection.—*A Plea for the Tuberculinization of Babies, R. C. Holt, Tubercle, November, 1920, ii, 54.*

A Simple Artificial Pneumothorax Apparatus.—The apparatus described was recently constructed at the Loomis Sanatorium as the result of several years of experimentation. All the good features of other types have been included; hence it is largely a modification of one or more well-known forms. The box, or container, is constructed of ¼-inch, double oak veneer. It measures 13½ inches high, 7¼ inches deep and 13 inches wide. The floor and vertical partition are of ½-inch pine. The apparatus operates on the principle of the siphon, the right-hand bottle being elevated to hasten the delivery of gas or air and lowered outside the case to create suction for filling. This bottle is elevated by means of a movable shelf supported at different levels by cleats. The bottles are 2-litre percolating jars, fitted with rubber stoppers and graduated in cubic centimetres. Each has 2 glass tubes, a long one and a short one. The rubber tubing connecting the bottles is slipped over the long tube of each. The fluid used is a compound solution of cresol, 1 per cent, which may be colored with alcoholic gentian violet or fuchsin. The stopcocks are a hard-rubber one between the jars, and a two-way metal cock, mounted on the side, near the manometer. The manometer consists of No. 3 glass tubing and is mounted by soft metal strips. It has a range of 14 cm. above and below the zero mark. The rubber tubing used has a $\frac{3}{16}$-inch lumen between the jars and a $\frac{5}{32}$-inch elsewhere. The box ready for use weighs 15 pounds. The filter consists of a glass cylinder fitted with a stopper and a long and short bent glass tube. It is nearly filled with 1:500 mercuric chloride solution. A small calcium chloride tube, with the bulb loosely packed with cotton, is attached to the longer tube. When the right-hand bottle is lowered and the cocks are opened, negative pressure is created in the left-hand bottle, and this in turn causes air to be drawn through the filter. This air (gas), having passed through cotton and bubbled through the mercuric chloride solution, is clean and presumably sterile, and is stored in the left-hand bottle until used. This method of filling has proved most satisfactory and can easily be done by the average nurse. The advantages of this apparatus are its ease of operation, lightness of weight (portability) and low cost. Any carpenter can construct the box or container, and the assembling and fitting up of the parts ought to be well within the powers of the average laboratory technician.—*A Simple Artificial Pneumothorax Apparatus, J. S. Woolley, J. Am. M. Ass., September 11, 1920, lxxv, 739.*

Hospital School for Surgical Tuberculosis in Children.—Surgical tuberculosis should be treated on open, barren, flat shores, which are exposed to the full force of the winds, and where an equable temperature, moderate humidity and abundant sunshine can be obtained. The hospital at Leasowe, England, is constructed on the block-pavilion principle, each block consisting of two stories with 24 or 30 beds on each floor. The wards face due south and are light and airy, with excellent cross-ventilation. On the southern aspect they are provided with large glass folding doors which open to roomy sun balconies. The treatment of surgical tuberculosis is carried out on conservative lines, and comprises the adoption of measures to arrest the disease and to carry out the orthopedic principles for the restoration of the function of the parts attacked. The treatment can be described as consisting of three stages: the acute, during which absolute physiological rest in the recumbent position, with immobilization of the diseased area, is demanded; the chronic, where recumbency is no longer compulsory, but immobilization must be maintained so as to allow repair to take place, and to prevent deformity; and the convalescent, during which complete immobilization is no longer necessary, and graduated exercises may be allowed. The duration of the respective stages, and that of the total time required to complete the treatment, vary in each case and are influenced by the virulence of theinfection, the site and extent of the disease, and the age and resisting powers of the patient. The most important adjuvant measure is heliotherapy. There can be no doubt as to its beneficial action The aim is to expose the whole body to the action of the sun's rays, and to produce a generalized pigmentation of the skin. The exposure is undertaken gradually so that tolerance may be acquired. The degree of pigmentation in some cases may be taken as an indication of the progress towards recovery. X-ray therapy and, more recently, chemotherapy have proved of valuable help in dealing with the more superficial manifestations of the disease. The combination of school work with the hospital treatment of these cases has proved a great success. Many of the children prior to admission have been unable to attend school for a considerable time, and being considered invalids they have become the spoilt tyrants of their homes. Their habits are unnatural; they are destructive, and often melancholic. Carefully planned work eliminates these tendencies, and the natural activities of the child can be directed into proper and healthy channels, and the monotony of the enforced recumbency relieved. The cases are followed to their homes after discharge from the hospital, and much valuable information is gained in confirming the diagnosis of cure and in watching the progress of these cases in after life.—*A Hospital School for the Treatment of Surgical Tuberculosis in Children, T. H. Martin, Brit. J. Tuberc., October, 1920, xiv, 145.*

Open-Air Schools During 1919.—The purpose of the open-air classes is to make it possible for types of pupils whose physical condition prevents them from attending school in regular classes to regain their normal physical condition and at the same time to procure their education without any loss of time. At present the following types of children are admitted: (1) Children exposed to tuberculosis at home or in whose family there has been a recent death from this disease. (2) Those who have had tuberculosis which is now cured. (3) Children suffering from malnutrition. (4) Those who become tired easily or show languor or fatigue before the end of the day and on this account are unable to carry on their class work. (5) Children suffering from nervous diseases except chorea. (6) Those who are frequently absent because of colds, bronchitis, etc. (7) Children suffering from cardiac disease who are recommended by the private physician as being proper cases for these classes.

Classes are located in public parks, roofs of schools and private buildings and in classrooms located in the public schools. There has been no difficulty in maintaining a full register in all the classes this year. The attendance was excellent, averaging much higher than the regular classes. Each child has a sleeping bag, cot and movable chair. Until the funds are available for better equipment it will be impossible to improve it. The medical inspectors examine every child at the beginning and end of each term and as often during the term as any individual child requires it. The nurses visit the classes at least once a week and keep the medical inspector informed as to the condition of the children. The follow-up work is conducted by school consultations, home visits and mothers' meetings. The qualifications of the teachers are good health, even temperament, capacity for doing a large amount of school work well, willingness to do social service and a desire to study the problems of this work. The classes observe the following daily routine: 9 to 10 a.m., school work; 10 to 10.15 a.m., extra feeding, consisting of 8 ounces of milk (the children are urged to bring bread or rolls and butter to eat with their milk); 10.15 to 11 a.m., school work; 11 to 12, rest period; 12 to 1 p.m., lunch period; 1 to 2.45 p.m., school work; 2.45 to 3 p.m., extra feeding as above. The number of applications received from physicians requesting that their patients be received to such a class is steadily increasing. Many must now be refused on account of the lack of classes. The number of school children exposed to tuberculosis in their homes is over 10,000, while the total capacity of all the classes is less than 3000. All the school work, except shop work and drawing, can be done in the open-air classes. Many problems remain unsolved. One of the biggest is to provide proper medical attention. At times it is difficult to get the parents to consent to having their children receive proper medical or surgical care for the defects found by the medical inspectors. In most cases, however, the parents agree to have their children attended to, but the facilities are not at hand. This applies especially to dental care. Another problem is the lack of special training of the new teachers. Many of the children need a prolonged stay in the country during the summer, but no places are available for such purposes. A school farm would solve this to some extent, as the children could do enough of the work to make it nearly self-supporting. Over 50 per cent of the gain made during the school session is lost during the summer vacations. The home conditions have received a great deal of attention, and the results are very satisfactory. The essentials of this work are fresh air, food, light, correction of physical defects that retard growth and development, and hygienic home and living conditions. No child is considered to have improved unless a gain of at least half a pound a month is made. The lower the temperature, the greater the gain. This seems to prove that it is not only fresh air that is required. This appears due to the fact that the appetite is remarkably increased during the cold weather. The school progress of the children in the open-air classes was excellent. In most instances the gain is lasting.—*Open-air Classes in the Public Schools of New York City during 1919, S. Josephine Baker and J. Sobel, Monthly Bull. Dept. of Health, N. Y. City, October, 1920, x, 225.*

Occupations for Consumptives. The old advice to seek a job in the open air and pursue it is still offered. There are no light jobs except those that bring light wages, and light wages mean a gradual but sure descent into poverty, malnutrition and misery. The unsuitability of most occupations is due to conditions inherent in all commercial occupations and undertakings. That the conditions can be altered with benefit to the consumptive, shows that it is not the trade per se that is injurious, but the manner in, and methods by, which it is carried on. Payment according to results, or piecework is a factor extremely detrimental to the consumptive. With diminished physical and mental force, but anxious to provide for himself and his family, he speeds up to such an extent that the work, although not actually laborious, produces a mental and physical fatigue distinctly harmful. Labor has no objection to the employment of consumptives in colonies, provided that certain labor-protecting stipulations are carried out. What it objects to is the possibility that consumptives may be trained and then thrown on to the labor market, there to obtain work for which a reduced wage may be paid by unscrupulous employers. After-care committees are now finding out how great are the difficulties not only of providing employment, but of obtaining the complex of conditions which make up a sheltered life. This complex consists of an environment free from a vitiated atmosphere, employment at a pace which obviates both mental and physical fatigue, economic conditions which allow of ample remuneration for part-time work, a mentality on the part of the patient to conserve his energy at play as well as at work, and to avoid excesses of all kinds. It is possible gradually to build up communities of consumptives where the complex of favorable conditions is available and where patients are enabled to do good work and earn good wages for an indefinite period. It is not known at present how long this period is. Accurate records are being kept and will be published when the numbers are greater and the length of time covered is sufficient to leave no doubt as to the fairness of the comparison. There is definite evidence that many trades, if carried out by consumptives under well-defined conditions, are of value as therapeutic agents. In many cases there need be no reëducation in a new and unaccustomed occupation. The trade itself must be adjusted to the man and not the man to the trade. Let his technical ability, often acquired during a long apprenticeship, have full play: it can never be replaced by a trade learned in later life, and the ease with which certain processes in his own trade may be accomplished makes it all the more suitable for the disabled man, provided the adverse conditions attaching to the trade are removed.—*Principles Involved in the Selection of Occupations for Consumptives, P. C. Varrier-Jones and G. S. Woodhead, Brit. J. Tuberc., October, 1920, xiv, 154.*

Treatment of Tuberculosis at the Seashore.—The article contains a résumé of the results obtained at the Asile Dollfus at Cannes, during the thirty years of its existence. Of some 1200 cases, comprising adenitis, ostitis, scrofulous skin changes, tracheobronchial and peritoneal tuberculosis, 51 per cent can be called cured, 41.7 per cent improved, and 7.3 per cent unsuccessful. Treatment consisted of sea baths, fresh air all the year round, and heliotherapy. The same effects are obtainable from radiation at sea level as in the higher altitudes. In cases of tracheobronchial lymphadenitis the marine cure is preferable to one at a greater altitude. However, if the lungs are infected, the baths may cause an awakening and spread of the disease.—*Le traitment de la tuberculose par la cure marine à l'Asile Dollfus (1886–1917), A. D'Espine, Rev. Méd. de la Suisse Rom., May, 1920, xl, 303.*

X-Ray Treatment of Tuberculous Lymphadenitis.—X-ray treatment is to be especially recommended in tuberculous adenitis in children and adolescents. Where no breaking down or liquefaction has yet taken place, early and brilliant results are the rule, and may be expected in over 80 per cent of all cases. In cases where some of the glands have broken down and are draining, this treatment will often produce early closure of the sinuses, reduction in size and softening of the scar tisssue and reduction in the size of the remaining glands. If at the beginning of treatment some of the glands are liquefied but not open and draining, it is frequently advisable to aspirate the contents by carefully drawing the fluid detritus into a hypodermic syringe through a moderate-sized needle, under the most careful aseptic precautions, and carefully sealing the small opening with collodion or benzoin. This aspiration may be repeated as often as fluid appears during the course of treatment. It is seldom necessary to do it more than two or three times. Suppuration is not considered to be a contraindication to X-ray treatment; in fact, numerous instances of remarkable cures of badly-suppurating cases, even after two to four operations, are reported in the literature and are upon the records of many roentgenotherapeutists. A very useful and efficient adjunct to the X-ray treatment, in cases where suppuration has continued for a long time, is the swabbing out of the sinuses with a mixture of equal parts of phenol and tincture of iodine. If the openings of the sinuses are too small to use a swab, a few drops may be instilled with a blunt hypodermic needle. Repeat this weekly. This will hasten the completion of the necrotic process until all the gland tissue is destroyed. It is advisable to apply a little sterile vaseline around the openings of the sinuses so treated, in order to protect the skin from the action of this mixture. The exact X-ray technique used must vary with the roentgenologist who is applying the treatment. An approved method is to give full dosage to all the affected area, about once every three weeks, using careful judgment as to what that dosage should be in each individual case. Just as it is in handling other active and powerful agents, each case must be treated as the indications of age, complexion, sensitiveness of the skin, and so forth, may indicate. Consequently, there can be no hard and fast rule laid down for the application of this treatment. One must study each case separately and determine its needs just as carefully as one would when applying surgical methods or administering drugs.—*X-Ray Treatment of Tuberculous Lymphadenitis, I. S. Trostler, Am. J. Clin. Med., December, 1920, xxvii, 804.*

Chemotherapy with Acid-Resisting Bacteria.—The authors became convinced that the active principle of chaulmoogra oil is in its acids, as they found it effectual in treatment of leprosy in a 2 per cent solution of the sodium salts. In the course of their research in this line they discovered that the nonsaturated acids in chaulmoogra and other oils possess the property of inhibiting the growth of acidresisting bacteria, and check the proliferation of the leprosy bacillus and the tubercle bacillus. They ascribe to this the benefit from chaulmoogra oil in leprosy and of cod liver oil in tuberculosis. These oils act as direct chemotherapeutic agents and not as stimulants for phagocytosis or as tonics. They tabulate the findings with various oils with which they treated cultures of various acidresistant bacteria. The chaulmoogra was the only oil which constantly prevented the development of the various microörganisms. Chaulmoogra oil derived from *Taraktogenus kurzii* was most potent. Patients with active pulmonary tuberculosis reacted to its acid salts as to tuberculin. The destruction of the bacteria in the tissues floods the system with toxic products from the dead bacilli so that the condition may apparently grow worse. This is less likely in leprosy as the bacteria are not so toxic. This is true also of cod liver oil in mild forms of gland, bone and joint tuberculosis.—*Ensaios de chimiotherapia sobre os germens acidos resistentes, A. Lindemberg & B. R. Pestana, Brazil-Medico, September 11, 1920, xxxiv, 603.*

Treatment of Hemoptysis.—It is important to get extravasated blood out of the lung. Coughing must be suppressed for fear of detaching the obstructing clot, but the blood and sputum must be expelled by cautious hawking. It is not necessary to keep the patient in bed if he moves about cautiously, unless there has been loss of over 100 cc. of blood, or there is fever. But even then it is not best for him to keep absolutely still. The necessity for ample feeding of the tuberculous patient must not be forgotten when he has hemoptysis. The anemia entailed by the hemorrhage must be combated. Primary fatal hemoptysis is extremely rare, but a clot may obstruct the vocal cords and can be removed by hand. In many cases the tendency to hemoptysis can be combated with calcium chlorid or an extract of blood platelets by the mouth. Even a teaspoonful of common salt swallowed dry or in solution will draw the blood to the digestive organs and thus lower the pressure in the lungs. The blood can be tied off in the limbs, but in this case the limbs must be released separately afterward, not all at once.—*Om Haemoptysenbebandling, E. Als, Ugeskr. f. Laeger, November 4, 1920, lxxxii, 1389.*

Camphor and Emetine in the Treatment of Hemoptysis.—Camphor in oil hypodermically has been recommended in the treatment of pulmonary tuberculosis. It has also been used for hemoptysis, but with varying results. The question is raised whether or not, when large doses are frequently repeated, it is not the oil, rather than the camphor, that does the good, in much the same way as gelatine when used subcutaneously. One author would divide hemoptyses into indirect or passive, and direct or active; the former being due to a congestion from cardiac insufficiency, and the latter being caused by progressive ulceration. The passive hemoptysis may be favorably influenced by camphor. There is a similar debate about the use of emetine. It would appear to be of greatest use in cases in which there is hypertension.—*Le Camphre et l'émétine dans lê traitment des hémoptysies, L. Cheinisse, Presse Méd., September 11, 1920, xxviii, 637.*

Silica in Pulmonary Tuberculosis.—Reference is made to the silica (SiO_2) content of various structures of the human body and to the effect of silicic acid in the treatment of various skin and other affections. A series of guinea pigs was given injections of colloidal silicic acid, after which they were infected with a pure culture of tubercle bacilli together with a number of controls. One-half of the silicic acid pigs developed intercurrent pneumonia several weeks later. No evidence of tuberculosis was found at autopsy. The other half, four months after infection with tubercle bacilli, showed no evidence of illness, whereas the controls showed definite tuberculosis after four to six weeks. A repetition of the experiment gave similar results, showing that guinea pigs may be protected against tuberculosis by means of injections of silicic acid. The author has treated patients for four years with silicic acid. The results have been published in a previous article. For the first three years a mixture of Herba Equisetimin., Herba Polygon., and Herba Galeopsidis was given in the form of a tea containing 43 to 272 mgm. of silicic acid per dose. More than four hundred cases in all stages of the disease are under observation. During the treatment, silicic acid is secreted in increased amounts in the urine. Hygienic-dietetic and other treatments are not discontinued. The conclusion is reached that after years of treatment with silicic acid the tuberculosis tends more towards a chronic indurative type. It has no direct effect upon the fever. Latterly, injections of 2 cc. of a 1 per cent colloidal solution of silicic acid are given every two days.—*Neue Probleme in der Behandlung der Lungentuberkulose mit besonderer Berücksichtigung der Kieselsäurefrage, A. Kühn, Zeitschr. f. Tuberk., September, 1920, xxxii, 321.*

Sodium Silicate by the Vein.—A deficiency in silica seems to be one of the factors in the predisposition to arteriosclerosis and to tuberculosis. The research here related shows that sodium silicate can be given by the vein at need without harm. The dose generally used was 2 cc. of a 1: 1000 solution, injected on alternate days, a total of ten injections; recommencing after suspension for a week or two. It was used for patients with arteriosclerosis, cardiorenal disease and angina pectoris as well as in tuberculosis. Among those improving under this treatment was one man of 53 confined to bed by the headache and vertigo of cerebral arteriosclerosis, who was restored to active life and can now read and walk without pains.—*Les injections intraveineuses de silicate de soude, L. Scheffler, A. Sartory & P. Pellissier, Presse Méd., November 10, 1920, lxxxii, 806.*

Treatment of Tuberculosis with Sodium Morrhuate.—Three cases of surgical tuberculosis, two of tuberculous lymph nodes and one of tuberculous caries of the ankle and elbow joints were treated. In both the former cases the nodes healed by first intention. They were given hypodermic injections of sodium morrhuate every four days, beginning with 0.5 cc. and raising it to 2 cc. gradually at the rate of 0.25 cc. every third time. They did very well under the treatment. Both put on weight rapidly and the fever disappeared. In advanced cases with distinct cavities in the lung, the treatment does not do much good. In the early cases with high and hectic type of fever, the improvement is marked and fairly rapid. The temperature begins to go down almost after the first two or three injections by slow degrees. The large hectic range between the low subnormal morning temperature and the high fever in the evening, begins to contract at both ends, until at the end of about 15 to 20 injections it steadies at normal or slightly above, throughout the day and night. The reduction in temperature is noticeable even in very advanced cases. There is generally a reactionary rise in temperature after each injection. The fall in temperature is gradual and lasts for about three days, so that if the injection is not repeated for five days the usual evening rise of the disease shows itself clearly. The injections are therefore repeated on the fourth day. With the fall in temperature there is simultaneous improvement in the cough and expectoration. The increase in weight is slow but marked. The maximum weight gained was about 2 pounds in a week. Half a pound in a week has been fairly common. The characteristic rapid pulse remains obstinate; night sweats and sleep improve with the fall in temperature. Marked changes were produced in the bacilli. The bacilli become beaded and broken, but in no case even after 80 injections did they disappear. This is a disappointing feature. The treatment though very promising needs backing with open air, good and nourishing food and tonics.—*Note on the Treatment of Tuberculosis with Sodium Morrhuate, G. R. Tambe, Tubercle, November, 1920, ii, 58.*

Curability of Tuberculous Meningitis.—The case reported concerns a man, thirty-two years of age, who except for influenza in November, 1918, had been well until February, 1919. The symptoms of influenza were headache, fever, dizziness and vomiting lasting about one week. The illness in February, 1919, began in about the same way. A little later diplopia, nystagmus, ptosis and facial paresis appeared with rigidity of the extremities and positive Babinski. He died July 16, 1919. After death tubercle bacilli were found in the spinal fluid. The autopsy showed tuberculous lymph nodes of the neck, caseous tubercles in the right pleura, tuberculous infiltration of the lung, caseous and calcified nodes in the mesentery, small grayish white firm nodules over the base of the meninges and a nodule in the left Sylvian fossa and on the surface of the cerebellum. There were evidences of a previous tuberculous meningitis and encephalitis with numerous tubercles on the surface of the brain and in the interior of the ventricles. These tubercles seemed chronic with a definite tendency to heal. This case is characterized by a certain definite chronicity. That the process at one time was exudative is indicated by the presence of scar-like areas in the membranes and thickening with hyalinization of the walls of the blood vessels. It may be concluded that tuberculous meningitis may heal, depending on the nature of the infection. It seems that this curable form of meningitis has occurred largely in persons who have suffered from chronic and relatively benign forms of tuberculosis. While about 60 per cent of all cases of tuberculous meningitis occur in the first two years of life and quite regularly result in death, the cases with recovery have occurred in older children and in adults. Tuberculous meningitis may heal without serious defects even when extensive lesions have formed.—*The Curability of Tuberculous Meningitis, F. Harbitz, Am. J. M. Sci., February, 1921, clxi, 212.*

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ABSTRACTS OF TUBERCULOSIS

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The Abstract Editor is Dr. George Mannheimer, 41 West 51st Street, New York City. Prompt transmission to him of reprints or abstracts of papers on tuberculosis, sanatorium or board of health reports, etc., will promote their early publication in this section.

Abstracts should be sent typewritten on one side of the page only. They should be as concise and compact as the subject matter of the article warrants. They should be headed with a short title, and followed by the full title of the paper, author's name, journal, date, column and page.

Tuberculosis Mortality in Vienna Before and After the War.—The war has completely upset demographic conditions in belligerent countries by the action of various causes, such as mobilization of men, emigration en masse of refugees, dietetic restrictions, etc. Figures show that in Vienna there has been a great increase in tuberculosis mortality in 1919, as compared with 1913–1914; the death rate in 1919 being comparable to that in 1892–1893. It is interesting to note that the increase has been much greater for women than for men, and the relative increase has been greater in the wealthier sections than in the poorer.

PER 10,000	GENERAL MORTALITY		TUBERCULOSIS MORTALITY	
	Men	Women	Men	Women
1913–1914	165	138	35.5	24.8
1919	213	215	54.5	52.3

—*La mortalité par tuberculose à Vienne avant et apres la guerre, L. Cheinisse, Presse méd., December 1, 1921, xxviii, 1611.*

Tuberculosis in Germany.—The death rate from tuberculosis in Prussia fell from 26 per 10,000 living inhabitants in 1892 to 13.8 in 1914 and rose to 22.8 in 1918. The increase as regards the whole of Germany is remarkable. Between 1914 and 1919, 100,000 more patients died than might have been expected, calculating from the rates of 1914. In 1913, there were 200,000 cases of lung tuberculosis; in 1918 this figure had risen to 340,000. The *Gesundheitsamt* estimates that there are at present little short of 500,000 cases in Germany. A similar rise in tuberculosis death rates and morbidity rates occurred in England during the war, but compared with the rates in 1892 it is not nearly so striking. An improvement took place in Germany as well as in England after the war. The highest death rate was reached in 1918. Improvement occurred especially in the second half of 1919 and has continued since. Whether the rates will shortly fall to the prewar level, is an open question, but taking into account the present food situation in Germany, it seems unlikely. The fact has to be faced that the present organization of antituberculosis work in Germany is unable to cope with the problem, because of lack of money, and because the German is no longer as docile and as amenable to health regulations as formerly. Besides, the dispensary system has not been effectively organized, especially in regard to treatment and aftertreatment. It is estimated by the *Gesundheitsamt* that only 25 per cent of any new series of cases can get effective sanatorium treatment and probably 50 per cent do not get adequate treatment.—*Tuberculosis in Germany, E. G. Glover, Lancet, April 2, 1921, cc, 715.*

Tuberculosis in New York City

Quarters Ending March 31, 1920 and 1921

		MANHATTAN	BRONX	BROOKLYN	QUEENS	RICHMOND	CITY
Population	1920	2,281,664	747,520	2,038,121	478,571	118,104	5,663,980
	1921	2,276,778	778,520	2,077,674	497,627	121,252	5,751,859
New cases	1920	1,982	406	1,074	178	46	3,686
	1921	1,654	331	817	172	49	3,023
Total cases in register	1920	14,064	3,472	6,741	1,565	266	26,108
	1921	14,502	3,439	6,588	1,436	316	26,281
New patients examined at clinics	1920	1,696	397	1,017	213	30	3,353
	1921	1,827	332	1,169	195	48	3,571
Total visits to clinics	1920	8,542	3,312	5,022	1,461	195	18,532
	1921	8,502	3,185	6,045	1,601	318	19,651
Cases under supervision	1920	108	173	346	1	5	633
	1921	156	56	428	12	10	662
Voluntary renovations	1920	228	85	129	8	30	480
	1921	177	42	42	301	42	604
Sputum examined	1920	5,717	1,701	2,559	509	101	10,584
	1921	5,437	1,371	2,537	536	79	9,960
Positive sputum	1920	1,094	208	487	111	15	1,915
	1921	915	192	442	114	11	1,674
Deaths	1920	899	231	621	151	37	1,939
	1921	708	149	457	96	37	1,447
Death rate per 1000 of population	1920	1.60	1.25	1.23	1.28	1.27	1.39
	1921	1.26	.78	.89	.78	1.24	1.02
Deaths, all forms of tuberculosis	1920	1,044	262	688	171	41	2,206
	1291	812	180	528	109	40	1,669
Death rate per 1000 of population	1920	1.86	1.42	1.37	1.45	1.41	1.58
	1921	1.45	.94	1.03	.89	1.34	1.18

—*Weekly Bull., Dept. Health, N. Y. City, June 4, 1921, x, 180.*

Mortality from Tuberculosis in Denmark.—Jensen compares the mortality by five year periods from 1890 to date in Copenhagen, in the various provinces, and for the whole country. The total mortality has dropped for the whole country by 31.05 per cent and in the mortality from pulmonary tuberculosis the decline has been 47.12 per cent. In the provinces, the corresponding figures are 29.49 and 54.10 per cent: in Copenhagen alone, 32.84 and 37.22 per cent. The total mortality for the whole country thirty years ago was 19.78 per thousand inhabitants; for the provinces alone, 19.013, and for Copenhagen, 20.782. The corresponding figures now are 13.639, 13.407, and 13.957.—*Tuberkulosedodeligheden, C. Jensen, Ugesk. f. Laeger, January 6, 1921, lxxxiii, 13.*

Deaths and Death Rates from Pulmonary Tuberculosis in New York City and State.—The following table, showing the deaths and death rates from pulmonary tuberculosis for New York City and State, for December, during the years 1913 to 1920, inclusive, is taken from the *Monthly Vital Statistics Review, New York State Department of Health, February, 1921, New Series, vol. i, no. 12.*

Pulmonary tuberculosis: Deaths and death rates, New York State and large subdivisions, December, 1913 to 1920*

MONTH	YEAR	NEW YORK STATE		NEW YORK CITY		REST OF STATE							
						Total		Urban		Rural		Institutional districts	
		Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
December average	1913–17	1,178	137.2	747	160.8	431	109.3	227	118.7	204	100.5		
December	1913	1,195	144.6	728	164.9	467	121.5	220	117.6	247	125.8		
December	1914	1,214	144.1	766	169.6	448	115.4	250	130.9	198	100.6		
December	1915	1,146	133.4	746	160.6	400	101.5	217	113.5	183	90.2		
December	1916	1,164	133.4	742	156.3	422	106.1	228	117.7	194	95.0		
December	1917	1,168	131.0	752	154.7	416	103.3	218	110.7	198	95.8		
December	1918	1,141	126.1	646	129.8	495	121.4	206	102.6	231	111.2	58	
December	1919	906	98.3	506	99.4	400	97.0	171	83.9	184	88.3	45	
December	1920	794	84.7	446	85.7	348	83.4	149	72.1	159	75.6	40	

* Deaths per 100,000 population per annum.

Social Prophylaxis against Tuberculosis.—The essential principle of all prophylaxis is the avoidance of contagion. Contagion is the necessary cause and other factors, such as community and family life, industry, the influence of alcoholism, only act in favoring contagion and in multiplying its sources and opportunities. The importance of infection is combatted by some who point out that 97 per cent of human adults are infected. The difference between those who are diseased and those who are merely infected is essentially a quantitative one, namely, the number of infecting bacilli. The lesser infections which remain latent are inevitable and need not concern us, but we should endeavor to suppress sources of open and abundant contagion. Many maintain that effort should be directed to strengthening the resistance of the individual, but while this is important, the chief factor is to combat the bacillus. Two main methods are indicated, placing a barrier of defense around the sowers of germs and a protection around healthy subjects. The former can be done by compulsory isolation of open cases and also by disinfection of the main source of danger, the sputum. The means of accomplishing this are (1) direct: dispensaries, sanatoria, special hospitals, child welfare, and finally, education; and (2) indirect: alimentary hygiene, the fight against alcohol, the bettering of living conditions, and hygiene in general. The rôle of the physician is most important. Not only must he make an early diagnosis, but also educate the patient and friends in prophylaxis. To do this successfully he, himself, must be convinced of the efficacy of the measures prescribed.—*La prophylaxie sociale de la tuberculose, L. Bernard, Presse méd., December 18, 1920, xxviii, 913.*

Campaign against Tuberculosis in Pennsylvania.—Established about thirty years ago, the Pennsylvania Tuberculosis Society was the first organization formed in this country for the purpose of arousing popular interest in the fight against tuberculosis and of promoting activities for the control and prevention of the disease. During the early years of its history the society worked in a quiet but persistent way. Papers on various phases of the tuberculosis problem were prepared, read and published. From time to time literature was issued for popular distribution. Opportunities were sought for presenting the subject to medical meetings and on other occasions. Efforts were made to arouse health authorities to a sense of their responsibilities in the matter of tuberculosis. The society gradually exerted an influence for tuberculosis prevention in many sections of the state. In 1908 the Pennsylvania society began to make itself known throughout the state. In that year the Christmas seal sale was first used as a method of raising funds for tuberculosis prevention work under the National Association. Since 1908 the Pennsylvania society has gradually developed at least something of an affiliated local organization in every county in the state except two. There are at present about a hundred of these local organizations. Many of them are strong county-wide tuberculosis societies, with paid full time secretaries, doing their work on a budget basis and in a business-like way. In many places the local organization is still a committee of a woman's club. In 1917 the funds of this state totaled about $95,000. There was no seal sale in 1918, when it was omitted at the request of the American Red Cross. But for that year's work throughout the country the Red Cross appropriated $2,500,000. Last year the amount raised for the Christmas sale, exclusive of Pittsburgh and Allegheny County, was nearly $300,000. The Pennsylvania Society confines its efforts very largely to a program of education and propaganda. It has endeavored to keep in line with the program for the country, outlined by the National Association, while at the same time taking into account conditions and needs of the state. It has not found it necessary to engage in clinic work because the state has maintained clinics in every county. Several other lines of activity have been included in the statewide program and in the program of most local organizations. These activities include efforts to make effective the medical examination of school children, periodical examination of industrial workers, education of the rural population through the granges, promotion of open air schools, introduction of the modern health crusade in public and parochial schools as a means of training the children in health habits, and publicity through the newspapers, schools and churches. Locally, the tuberculosis organizations of the state have given exhibits and assisted in maintaining health centres clinics, community nurses and sanatoria; and they have made surveys, and provided nursing service. Much attention is being given to the need for hospital accomodation for advanced cases. The society endeavors to keep before the local organizations the importance of finding early cases, early examination, placing advanced cases in hospitals, care of contacts, training of children in health habits, provision of clinics, sanatoria, open air schools and nurses and general education on tuberculosis prevention.—*The Educational Campaign Against Tuberculosis in Pennsylvania, A. M. Dewees, N. York M. J., April 20, 1921, cxiii, 608.*

Stigmata of Predisposition to Bone and Joint Tubercle.—An exhaustive review of the literature shows: (1) that persons of red or light colored hair are said to be peculiarly subject to bone and joint tubercle, as well as to other forms of tuberculosis; (2) that there is first a certain pallor—not that present in the developed disease but antecedent to it,—such pallor being a possible sign of weakness due perhaps to deficient food, faulty hygiene, debilitating diseases, trauma, and the like; (3) that an increased access to external noxae is produced by heightened permeability arising chiefly from thinness of the skin,—a view substantiated by Cornet's observation that by rubbing cultures into the skin, tubercle bacilli could be made to traverse unbroken skin without leaving a trace of their passage through it, and to provoke reaction in the corresponding lymph nodes; (4) that ichthyosis predisposes to tubercle; and (5) that there are two nontuberculous nasal affections eminently characteristic of scrofula and surgical tubercle—chronic catarrhal rhinitis and ozena.

Comparison of subjects of bone and joint tubercle with normals

Red hair

Patients with tuberculous bone or joint	7.0% of 353 cases
Normal controls	3.4% of 610 cases

Freckling

Tuberculous	65%	5%
Control	57%	3%

Dental caries

Tuberculous	No significant difference
Control	

Ichthyosis

421 total tuberculous cases (male 244, female 177)	7 cases, 1.4%
324 nontuberculous cases	2 cases, 0.6%

Further stigmata of predisposition to bone and joint tuberculosis

Ozena

In 404 tuberculous cases	0
In 573 controls	2

Simple atrophic rhinitis

In 404 tuberculous cases	16 cases (3.9%)
In 573 controls	17 cases (2.9%)

Nasal obstruction

In 404 tuberculous cases	92 cases (23.0%)
In 573 controls	45 cases (6.2%)

Mentally defective (excluding idiots)

In 350 tuberculous cases	6 cases (1.4%)
In controls from several large schools Average	0.5%

Hypertrichosis

In 246 tuberculous cases	6 cases (2.4%)
In 181 normal school boys	1 case (0.5%)

Squint was found to occur more frequently in tuberculous than in normal adults, but less frequently in tuberculous than in normal chlidren; so that squint may indicate predisposition to adult pulmonary, but not to juvenile osseous tubercle.

The above figures indicate that red hair, freckling, ichthyosis, simple atrophic rhinitis, nasal obstruction, mental deficiency, and hypertrichosis, are stigmata of predisposition to juvenile bone and joint tubercle.—*Stigmata of Predisposition to Bone and Joint Tubercle, W. C. Rivers, Brit. J. Child. Dis., April, July, and October, 1920, xvii, 59, 140, 179.*

Metropolitan Life Insurance Company Sanatorium.—A total of 802 patients was admitted to the Sanatorium during the past two years, while 774 were discharged. Among the tuberculous patients admitted there has been a very satisfactory percentage—64.85—of incipient cases. Of the 342 tuberculous patients discharged during this period, 285 or 83.33 per cent returned to their homes improved, while only 57 or 16.67 per cent were classed as unimproved, or had died. Following such an extensive and devitalizing disease as influenza, it was almost certain that many postinfluenzal cases should be brought to the Sanatorium for study and treatment. Careful questioning has been made of all patients admitted since the epidemic started, to determine whether they had a disease that could be properly termed influenza. It was found that of the admissions during 1919, 154 patients gave a history of having had influenza, and of this number 68 were diagnosed as tuberculous when admitted. Among the majority of the postinfluenza cases, however, tuberculosis was not found to be present, although in many of them a diagnosis of that disease had been made before admission.

Classification of tuberculous patients admitted to the Sanatorium during 1914, 1915, 1916, 1917, 1918, 1919 and 1920:

	1914		1915		1916	
		per cent		*per cent*		*per cent*
Incipient	27	27	69	43.67	127	55.46
Moderately advanced	63	63	83	52.53	92	40.17
Far advanced	10	10	6	3.80	10	4.37
	100	100	158	100.0	229	100.0

	1917		1918		1919	
Incipient	146	66.37	77	52.74	126	66.32
Moderately advanced	69	31.36	62	42.46	48	25.26
Far advanced	5	2.27	7	4.80	16	8.42
	220	100.0	146	100.0	190	100.0

	1920	
		per cent
Suspected tuberculosis	7	4.37
Incipient	101	63.13
Moderately advanced	40	25.00
Far advanced	8	5.00
Surgical tuberculosis	4	2.50
	160	100.0

—*Metropolitan Life Insurance Company Sanatorium. Report for 1919 and 1920.*

Influence of Trauma on Surgical Tuberculosis.—The question of the influence of trauma on tuberculosis is a difficult one, from the scientific point of view and even more from the practical standpoint, and it often embarasses the physician who is obliged to testify in accident and industrial cases. There undoubtedly exist cases caused directly by trauma, but they are very rare, as for example, those arising from direct inoculation. But almost always the physician is consulted for lesions, most frequently of bones or joints, which are attributed to a contusion or previous sprain. This tendency is due to the fact that it offers a simple pathogenesis and satisfies the desire to attribute misfortune to external causes. One must learn not to attribute to traumatism what is the result of an industrial disease. The previous state of the patient, his habits and the effect of his work on his health must be inquired into, in order to determine whether the accident did not simply reactivate an old lesion. Often one finds out that certain motions were less free or that one leg became tired more easily. On examination one finds a slight muscular atrophy or an adenopathy. If one inquires precisely into the relative dates of the evolution of the lesion and the accident a flaw is often discovered. The fault of correlation is relatively easy to discover, if the traumatism is recent and the lesion an old one, or if the traumatism is old and the lesions recent; but in cases where they are of about the same age it may be very difficult. Broca, while not denying absolutely the possibility of violence being the origin of a tuberculous lesion, believes it to occur only in exceptional cases. Five hundred children with trauma have been followed for a considerable time, none of them having developed the disease. Trauma without a wound cannot originate tuberculosis. It is a clinical fact that a known trauma in a known pretuberculous person almost never is the origin of a tuberculous lesion. Concerning the influence of trauma on osteoarticular tuberculosis, there is no doubt that any trauma is an aggravating factor. From the practical standpoint it is therefore very important to know the condition of the patient before the accident. Another mode of traumatism, the consequences of which it is equally important to know is that which follows straightening of faulty positions due to white swelling. This may produce local reactivation and even generalized tuberculosis with meningitis.—*Influence du traumatisme sur la tuberculose chirurgicale, A. Broca, Progr. Méd., February 26, 1921, no. 9, 91*

Nitrous Oxide-Oxygen Anesthesia in Tuberculous Animals. Due to the great prevalence of pulmonary tuberculosis, an anesthetic that can be used for operative procedures on tuberculous individuals, without producing injury to them, is greatly needed. Only during the last few years has it been fully recognized that a rapid spread of the disease often followed operations on the tuberculous under ether anesthesia, and for this reason clinicians treating cases of tuberculosis generally advised against surgical intervention except under extreme circumstances. Corper, Brown and Petroff, and Rogers showed that repeated ether anesthesia on infected animals does not result in a more rapid spread of the disease process. The conclusion seems warranted that the detrimental influence of ether anesthesia results from purely mechanical factors, and is due largely to aspiration from the apical lesion, usually a cavity, to other areas of the lung, causing aspiration bronchopneumonia. Ether anesthesia not only causes labored respiration but increases the secretions, diluting the infectious sputum, and in this way causes a general spreading of the bacteria. Since nitrous oxide and oxygen are less irritating, Rogers performed experiments to determine their effect on laboratory animals artificially infected with tubercle bacilli. Since animals rarely develop the chronic ulcerative type of tuberculosis an exact comparison cannot be made. Thirty-seven male guinea pigs were infected with active tuberculosis: 20 of these were given repeated nitrous oxide-oxygen anesthesia. In one experiment 8 of the 13 controls died from pneumonia before the experiment was completed, while only 3 of the 13 nitrous oxide animals died during the experiment. Of the 4 controls which died after fourteen days all showed tuberculosis of the lungs, liver, spleen and bronchial glands. When the 10 treated and the 4 remaining controls were dissected thirty days after infection, no difference could be noted in the anatomic distribution or extent of their tuberculosis. In the second experiment, the disease was permitted to develop fourteen days and the animals then treated with the gas every fourteen days. Immediately following the last anesthesia, both the experimental and the control animals were killed and sectioned. There was no difference in the amount of involvement in the anesthetized and the control animals. It is therefore concluded that nitrous oxide-oxygen anesthesia, administered daily to guinea pigs suffering from pulmonary tuberculosis, does not influence the development of the disease, neither is it detrimental to the general health of the animal. Since these gases interfere less with respiration and irritate less than ether, they are more suitable for anesthesia in cases of pulmonary tuberculosis and other respiratory diseases. —*Studies in the Effects of Nitrous Oxide-Oxygen Anesthesia on Animals Infected with Tuberculosis through the Respiratory Tract, J. B. Rogers, Am. J. Surg., April, 1921, xxxv*, 44.

Diagnosis and Prognosis of Tuberculosis in Infancy.—In 661 consecutive autopsies on children under two years, at the Infants' Hospital, Boston, 138, 20 per cent, showed tuberculous lesions,—which suggests how often the disease is overlooked clinically. The clinical diagnosis of tuberculosis in infancy is usually based on the existence of the secondary stage of the disease, as for example tuberculous meningitis or bronchopneumonia. Moreover, it is often impossible to tell before autopsy whether the bronchopneumonia is due to the tubercle bacillus or to other organisms. In 374 cases a clinical diagnosis of tuberculosis was made with the following result:

Analysis of 374 cases

	Cases
Diagnosis of tuberculosis made...	374
Total admissions to hospital in same period..................	3100
Diagnosis confirmed..............	291
Diagnosis confirmed by necropsy.	129
Total necropsies in same period...	661
Diagnosis confirmed by subsequent clinical developments....	153
Diagnosis remained unconfirmed.	78
Diagnosis contradicted by necropsy findings..............	5
Diagnosis not made clinically in cases found tuberculous at necropsy....................	9

The frequency of clinical tuberculosis in hospital patients under two years of age is shown by the fact that tuberculosis was diagnosed in 12 per cent of all admissions, and confirmed in 9 per cent. The diagnosis was considered confirmed when tuberculous lesions were found at necropsy or when unmistakable clinical types of the disease developed. No pulmonary manifestation was considered "unmistakable." A diagnosis of tuberculosis was not made unless one of three signs was present: positive Pirquet, interscapular dulness, and d'Espine's sign, and the roentgenogram. Of course, a diagnosis of tuberculous meningitis required confirmation by lumbar puncture. Of the 374 cases, the Pirquet was positive in 181, negative in 111, questionable in 11. The high percentage of negatives is to be explained by the frequency of marked atrophy and anemia. A negative Pirquet in no way rules out tuberculosis in an infant under two years of age. A positive Pirquet at this age is, however, sufficient evidence for a positive diagnosis of tuberculosis. In the primary stage of the disease, a diagnosis of tuberculosis based on a positive d'Espine's sign or on interscapular dulness, or both, will be right in the majority of cases. A negative finding does not rule but tuberculosis. Greatest reliance was placed on the examination of roentgenograms of the chest. The primary lesion is usually not shown, but enlargement and caseation of the bronchial nodes can be seen. Acute miliary tuberculosis of the lungs can usually not be demonstrated. Tuberculous bronchopneumonia invariably shows in roentgenograms, though not always recognizable as tuberculous. Roentgenograms of the chest were positive in 70 per cent of the cases; positive or suspicious in 89 per cent; and negative in 11 per cent.

Outcome in 369 cases diagnosed as tuberculosis

	Cases
Died in hospital	194
Discharged living	175
Present condition unknown	50
Present condition known	125
Died after discharge	82
Alive and well	43

The tendency to develop the fatal forms of the secondary stage is greatest in infancy, and grows less as the child grows older.—*The Diagnosis and Prognosis of Tuberculosis in Infancy, C. H, Dunn and S. A. Cohen, Am. J. Dis. Child., February, 1921, xxi,* 187.

Surgical Tuberculosis in Infants.—In a thirty years' pediatrics experience no cases of mesenteric adenopathy, or of tuberculous peritonitis in infancy, were seen. Multiple disseminated subcutaneous abscesses were found to be quite common in infants, the growth of pyogenic organisms being favored by the presence of tuberculosis. Subcutaneous gummata were so frequent as to be an excellent sign of tuberculous impregnation. Only one or two cases of tuberculosis of the lymphatics were found in nurslings, the process being commoner after the first year. Tuberculous infection of the epididymis and testicle was found in several cases six months to two years of age. One case of cervical Pott's disease and one of middorsal Pott's in babies eleven and twenty-one months old; one case of tuberculous knee-joint in an infant of thirteen months, and two others in infants twenty-one months old, each, are reported. Mention is made of a dozen cases of tuberculous rickets, emphasized that this does not mean rickets being in tuberculous infants.—*Brief Considerations of Surgical Tuberculosis in Infants, C. G. Cumston, Brit. J. Child. Dis., October to December, 1920, xvii, 189.*

Tuberculosis in Infants and Young Children.—Of 8,919 sick children admitted to the Babies' Hospital (New York) between April 1, 1914 and April 1, 1920, 359, or 4 per cent had symptoms of tuberculosis in some form. Three others had tuberculous lesions at necropsy which had not been suspected during life. Of 2024 necropsies performed during these six years, 184, or 9 per cent were on tuberculous subjects. In 1909 this percentage was 13. In 1914 it was 16. The total death rate for all admissions to the Babies' Hospital had decreased, while the death rate for cases of tuberculosis has increased. More tuberculous patients were admitted between February and June than during the second half of the year. Their number increases as that of other respiratory infections subsides, the tuberculous infection probably being lighted up by preceding acute respiratory troubles. A definite history of exposure was obtained for only 94 of the 362 children. Twenty-two of 29 children whose mothers were tuberculous died before they were one year old, 6 died in second year and 1 in the third. Only 16 of the 37 whose fathers had tuberculosis died before they were one year old. The 362 children ranged from six weeks to five years. The greatest frequency was noted in children between six and twelve months of age. Two hundred and sixty-nine, or 74 per cent, gave a positive Pirquet reaction. Fifty did not react. In 43 cases the reaction was not recorded.

Clinical forldins:	*Cases*
Tuberculous meningitis	193
Pulmonary and general miliary tuberculosis	116
Tuberculous peritonitis	28
Tuberculosis of the bones	12
Tuberculous cervical adenitis	10
Intestinal tuberculosis without peritonitis	2
Tuberculosis of the penis and inguinal glands	1
Total	362

Clinical forms:

Tuberculosis primary in the respiratory tract:	
Cases with oldest lesion in lungs	74
Calcareous areas in lungs	3
Cavities	40
Primary lesion in left upper lobe	16
Primary lesion in right upper lobe	17
Primary lesion in right lower lobe	13
Primary lesion in left lower lobe	16
Primary lesion in right middle lobe	11
Primary lesion in bronchial nodes	57
Tuberculosis primary in the digestive tract	9

Tuberculous meningitis was present in 53 per cent of cases in this series. None recovered. Thirty-nine per cent were under one year; 76 per cent were under 2 years. Necropsies were performed in 123 cases. In 116 the primary lesion was found in the respiratory tract, in the intestines and mesenteric nodes. In babies under six months old, the average number of organs containing tuberculous lesions was 9. There were 28 cases of tuberculous peritonitis. Only 5 came to necropsy. Laparotomy was done on 3 cases, and tuberculous masses were reported in the abdomen of each. The heart is rarely involved in tuberculosis of young children. Exudative tuberculous pericarditis is very rare, occurring in 1 case among the 184 necropsies studied. Tuberculides were found in only 4 cases of the series. All had a very generalized tuberculosis. The 3 youngest died of tuberculous meningitis.—*A Study of Tuberculosis in Infants and Young Children, Martha Wollstein and R. C. Spence, Am. J. Dis. Child., January, 1921, xxi, 48.*

Tuberculosis of Children.—Hans Much has for a number of years been the chief exponent of absolute immunization against infection. Not many men are willing to support Much in his premise that an absolute immunity against tuberculosis can be secured. Most physicians will agree to a relative immunity; a few would be unwilling even to admit this; but not many American physicians will follow Much in his extreme point of view. Of course, it should be borne in mind that Much is dealing largely with the problem of tuberculosis in children and of childhood infection. He believes that the fight against tuberculosis should be carried on chiefly in its greatest stronghold—childhood. "Tuberculosis in childhood must be cured," he says, "Practically nothing has been done before. Our method of campaign up to date has been entirely wrong." As to the treatment: "It must be expected that the cure of tuberculosis is entirely dependent upon immunity. When properly used, chemical, physical, dietetic, or surgical measures all have the one purpose: to improve the immunity and thereby to conquer the disease." Based upon these assumptions Much has developed a form of treatment which he calls the partigen (partial antigens) treatment. He is also very emphatic in his belief that no tuberculin, no serum, no specific method of any kind is of use that does not take into consideration all of the antigens.—*Tuberculosis of Children, by Dr. Hans Much, Director of the Department for the Science of Immunity and for Tuberculosis Research, University of Hamburg, Germany. Translated by Dr. Max Rothschild, San Francisco. Published by MacMillan Company, 1921, 156 pp.*

Course of the Tubercle Bacillus from Sputum to Child.—That human sputum is the chief source of tuberculous infection is generally admitted, but there is considerable divergence of opinion concerning the immediate medium of infection. The hypotheses of Cornet, Flügge and Aufrecht have gained the widest acceptance. According to Cornet and Flügge infection takes place almost exclusively indoors, either by indirect infection or direct from person to person. Both viewed raw sputum as insignificant. According to the third hypothesis, everything containing tubercle bacilli and passing human lips can set up an infection either by inhalation or by ingestion. Tuberculous sputum can arouse infection, whether inhaled or ingested as suspension, spray or dust or in its natural crude condition. The early rapid tuberculization of the species is an established fact. In many young children the source of infection cannot be traced, if the direct contact with coughing consumptives is taken as a *sine qua non*. About 10 per cent of children exhibit infection by the end of their second year; at three years from 15 to 20 per cent; by six years from 50 to 60 per cent; and by 15 about 75 per cent. Most children spend a larger part of their time out-of-doors at the period from four to seven than at any other period of life. Infants come into closest physical contact over long period with certain individuals and live largely on milk, perhaps cow's milk; yet the total result is an infection incidence of only 10 to 20 per cent. It seems amazingly small; yet it probably represents the relative importance of dust plus droplet plus cow's milk in the scheme of tuberculous infection. We cannot explain infection scientifically; yet the most abundant immediate source of tuberculous infection should be given its due place. Raw sputum, recently expectorated, bespatters the streets everywhere, and the floors in too many places. Children at home live and play close to the floor; outdoors they engage for the most part in "ground" games. Doing so, they cannot help attaching to their hands the offal of sidewalks and streets and with this, the sputum of many people, and since few children have developed a conscience about putting their hands into their mouths, considerable raw sputum will find its way there. Cervical lymphadenitis is the most frequent manifestation of clinical tuberculosis between the ages of three and ten. Foci in the neck nodes undoubtedly represent infections that occurred by way of mouth or nose. Studying large series of cases, observers have been able to detect a tuberculous infection incidence of 5 per cent in tonsils and adenoids which showed no gross evidence of tubercle. This 5 per cent must be regarded as the minimum of tonsillar and adenoid infection in the patients in question. This high incidence of nasopharyngeal and cervical infection in childhood should establish a common locus of early infection. —*The Course of the Tubercle Bacillus from Sputum to the Child, A. K. Krause, N. Y. State J. of Med., March, 1921, xxi, 83.*

Apex, Hilum and Lower Lobe Lesions of Tuberculosis in Childhood.—From evidence reviewed it appears probable that in the young child there exists a physiologic cause which predisposes the hilum of the lungs to tuberculous infection, namely, the low resistance to tubercle toxin and the consequently greater dependence on the lymphatic system to combat the infection. On the other hand, there is an anatomic cause for the comparative immunity to infection of the lung apex, in the greater respiratory excursion and freer circulation in the child as compared with the adult. In accordance with these phenomena, tuberculosis in the child may be diagnosed most frequently at the hilum, the apex being next in frequency, and the base least often.—*Apex, Hilum and Lower Lobe Lesions of Tuberculosis in Childhood: Their Relative Frequency, W. R. Vis, J. Am. M. Ass., April 23, 1921, lxxvi, 1156.*

Radiologic Diagnosis of Pulmonary and Glandular Tuberculosis in Children.—Clinical diagnosis of thoracic glandular tuberculosis in infants should in all cases be confirmed by radiologic examination. The latter clears up, especially the condition of the hilum and the mediastinum. In the frontal position the shadows of the hilum overlap the mediastinal shadows to the right and to the left, while the central shadow represents the projection of the sternum, the large vessels and the spine. We recognize three stages of hilum disease. In the first stage the shadows hardly extend beyond one or two intercostal spaces, the right one being more extensive and apparent than the left; in the second stage the shadows of the hilum are more entangled with the adjacent shadows and always more hazy, and tend to resemble stumps. Sometimes there are clear areas on each side of the median shadow which gives the general appearance of a butterfly with its wings spread out, although this characteristic may be unilateral. In the third stage, the shadows of the hilum are clear cut, their ramifications are darker and are reinforced by small calcifications, either grouped in small constellations or scattered. They are more extensive and may reach as high as the clavicle or down to the diaphragm. Sometimes there are present aberrant or isolated calcifications quite removed from the hilum, either at the bases or in the lateral portions or in fact anywhere in the chest. These take on a peculiar significance. It has been argued by Ribadeau-Dumas and Debré that the primary infection of pulmonary tuberculosis in infancy is marked by a tubercle varying in size from a pin point to that of a pea, located frequently subpleural in one of the lower lobes. This "tuberculous chancre" may become the origin of tracheobronchial adenopathy.—*La diagnostic radiologique de la noberculose ganglio-pulmonaire chez l'enfant, H. Mery, G. Detre, and A. Mezmoulins, Presse méd., March 19, 1921, xxix, 221.*

Chronic Tuberculous Hilum Pneumonia in Children.—Summary: 1. Extensive tuberculous lesions about the hilum, which pursue a rather chronic course, may may occur in infants and young children. (2) Recovery probably takes place in the majority of these cases even in children under two years of age. (3) The onset in this type of pulmonary tuberculosis is more or less gradual and there may be no lung signs until after the disease has lasted for some time. (4) Irregular fever, sweating, expiratory obstruction, diminished breathing, with impaired resonance, a positive Pirquet and a characteristic roentgen ray picture are among the earlier manifestations. (5) Enlargement of the supraclavicular lymph nodes, positive results from guinea pig incoulation of material from lung puncture or of sputum, and the presence of tubercle bacilli in the sputum may be found later in the course of the disease. (6) Given an infant or child with prolonged irreguar fever and sweating, showing a positive Pirquet, this form of tuberculosis should be suspected and its further early manifestations sought for.—*Chronic Tuberculous Hilus Pneumonia in Children, D. Greenberg, Am. J. Dis. Child., January, 1921, xxi, 65.*

Complement Fixation for Tuberculosis in Children.—The results of 1855 tests on 1556 children are given. In manifest tuberculosis there was a striking relation between the age of the child and a positive fixation reaction. More than eighty per cent of those over six years of age gave positive reactions, while none in the first year reacted positively. The younger children may have had the infection too short a time for the development of complement-fixing antibodies: or, more likely, young animals may form antibodies much less readily than older ones. This may have some relation to the rapid spread of the disease at this time of life. Thus, in younger children the skin test means more and the fixation test less. In older children the reverse is the case. The fixation test is of great aid in the diagnosis of masked juvenile tuberculosis, that is, active, pathological tuberculosis which does not produce well defined clinical symptoms. Such a conditon, though it may at first escape detection by careful physical examination, may in some cases produce an active, readily recognizable tuberculosis. No patient giving a positive reaction should be considered free from active tuberculosis without a thorough study.—*Complement Fixation for Tuberculosis in Children, J. V. Cooke, Am. J. Dis. Child., January, 1921, xxi, 78.*

Early Diagnosis of Tuberculosis of the Tracheobronchial Glands in Children.—Tuberculosis of the tracheobronchial nodes is the predominant lesion in children and much more important than pulmonary tuberculosis. For this reason early diagnosis is most important so that proper treatment can be instituted. These nodes are the starting point for the distribution of bacilli to other organs and probalby for the invasion of the lung by a retrograde route. The family and personal histories are of importance but only clinical examination and careful study of the physical signs can give exact information. The examination should be commenced by looking for general symptoms arising from a possible tuberculization of the organism: loss of weight, pallor, enlargement of cervical, axillary or inguinal nodes, etc. Then inquiry is made as to functional symptoms, especially cough, harsh, dry, and spasmodic. In the physical examination inspection does not furnish much help except when revealing enlarged veins on the front of the chest. Percussion may reveal altered resonance in the parasternal regions, such changes being more easily made out in front than posteriorly. In contradistinction to this the changes found on auscultation are more marked behind than in front and consist in modifications of breath sounds or of the transmitted voice. D'Espine's sign is of marked significance, as is also the feeble inspiration which extends out beyond the hilum, sometimes over the greater part of a lung. Some authors dispute the importance of this feeble inspiration but there is general agreement as to the significance of rough and low inspiration (inspiration rude et basse). In addition to the more permanent râles there may be transitory adventitious sounds caused by congestion in the neighboring lung tissue. The clinical examination should be controlled by X-rays and, if possible, tuberculin reactions.—*Le diagnostic clinique précoce de la tuberculose gangliopulmonaire chez l'enfant, H. Méry, Presse méd., December 4, 1920, xxviii, 873.*

Quasi-Continuous Temperature Records in Early Diagnosis.—The quasi-continuous (half minute) temperature record is a valuable diagnostic indication of the tuberculous nature of the disease, the activity of the process and the prognosis. While the temperature may give some indication of the tuberculous nature of the type of the disease, such as acute miliary tuberculosis, caseous pneumonia and the chronic fibroid type, the physical signs afford considerably more specific information. The temperature indications as to the resistance or lack of resistance of the tissues of the patient are of extreme interest, especially in regard to prognosis. Instability of the temperature affords evidence of a high toxic absorption, ready reaction of the tissues to the toxic stimulation and marked interference with the rest function of the patient. A restless night is reflected in the temperature curve, and it appears that the inverse temperature is to a large extent the result of a continued autoinoculation, during which a minimum stimulus produces a maximum reaction, both as to amount and duration. The features in these quasi-continuous records on which stress is laid as being of diagnostic value are somewhat sudden rise of the afternoon and evening temperature, not necessarily steady, but in jerks and with a general trend upwards; continuation at a relatively high level, above 99°F. for eight or ten hours, followed by a rapid fall, sometimes to a subnormal level; during the whole day, response of the temperature to agents inducing rise or fall: exercise, food, cold or warm drinks, much more readily and through a much wider range than in the healthy individual. A combination of certain of these is called a plateau, namely, a long continued temperature above 99° F. commencing with a sudden rise and ending with a sudden and prolonged descent. This is pathognomonic of tuberculosis. In all the authors' doubtful cases in which the patient ultimately did badly, this plateau temperature curve developed during the early stage of the disease. An account is given of 9 cases and a record of 23 charts which form corroborative evidence of the diagnostic and prognostic value of these records. In the night sweats there is evidence of some interference with autonomic nerve centres, leading to dilatation of the surface blood vessels, great radiation of heat from the cutaneous surface and rapid lowering of the temperature. A series of temperatures taken by mouth bore little relation to the rectal temperatures. They give little indication of the extent or progress of the disease, or in its earlier stages, of its presence.—*The value of the Quasi-Continuous Temperature Record in the Early Diagnosis and Prognosis of Tuberculosis, G. Woodhead and P. C. Varrier-Jones, Lancet, March 19, 1921, cc, 573.*

Presumptive Evidence Furnished by the Habitus and the Skin.—There are a certain number of signs drawn from the habitus of a person which indicate a tuberculosis predisposition or the beginning of an invasion: slender bones, slight development of the musculature in general and atrophy of certain groups of muscles, especially the trapezial and the pectorals, long narrow chest and winged scapulae. Myoedema of the pectorals is found in the cachectic, in convalescents from cholera or typhoid fever, and in the cancerous. The cheeks are flushed, the eyes moist and the corneae transparent bluish. Individuals with red hair were considered to be predisposed by Hippocrates. As a matter of fact it is the "partially red," as for example those with black hair, but red beard and red pubic hair who seem most predisposed. According to Queyrat's statistics, there were only 3 tuberculous out of 12 with complete red hair, but out of 56 individuals who were partially red 52 were tuberculous. The relation between a hypertrichosis and the development of tuberculosis has long been noted. Cervicodorsal or interscapular hypertrichosis is of the greatest importance. Changes in the nails which become thinner, less resistant, more fragile or show transverse ridges, are characteristic. The skin becomes pale, often dry; there may be keratosis pilaris or xeroderma, particularly in the region of the posterior brachial region. In later stages the skin desquamates. Hyperplasia of the mammary glands is noticed in girls. Certain cicatrices are characteristic. Tuberculous sores are more or less deep, irregular, crossed by filaments generally adherent to the underlying tissues and often keloid. Fragments of keloid inoculated into guinea pigs produced tuberculosis. The retraction of the palmar aponeurosis—Dupuytren's disease—may be considered presumptive evidence of tuberculosis. Very large tonsils are suspicious, as is a red line on the gums. Certain dermatopathies are found in the tuberculous, exclusive of the frankly tuberculous lesions, namely, pityriasis versicolor, keratosis pilaris, a number of eczemas, lichen scrofulosorum, parapsoriasis of Brocq, interscapular telangiectases, hyperpigmentations, angiokeratomata and purpuric spots.—*Présomptions de tuberculose tirées de l'habitus exterieur et de l'examen de la peau, E. Queyrat, Progr. Méd., November 6, 1920, no. 45, 487.*

X-Ray in Diagnosis.—At the Municipal Tuberculosis Sanatorium, Chicago, 1236 chests were examined stereoscopically in 1920 and 1431 chests were fluoroscoped. These examinations helped very materially in differential diagnosis, in establishing the indications for pneumothorax treatment and as a guide during the course of such treatment, in affording an opportunity for the study of the topography of the lesion and in determining its activity, in the diagnosis of latent lesions and in the diagnosis of pulmonary lesions at the very beginning.—*The X-Ray in the Diagnosis of Pulmonary Tuberculosis, A. J. Hruby, Am. J. Clin. Med., April, 1921, xxviii, 228.*

The Urochromogen Reaction in Surgical Tuberculosis.—Klare has been applying the urochromogen test in all his cases of surgical tuberculosis for the last two years, and reports that what Weiss states in regard to the significance of urochromogen in pulmonary tuberculosis holds good in the main for surgical tuberculosis. The continual demonstration of urochromogen is to be regarded as indicating a very unfavorable prognosis, and while patients presenting a transitory urochromogen reaction may live for several years they have no prospects of recovery. Thirty of his cases (18 soldiers and 12 children) gave a positive urochromogen reaction. Of the 18 soldiers, 12 died within a year; and the others 6 have not improved. Of the 12 children, 4 died within a year; the condition of the other 8 is either unchanged or worse. In only one case has there been any improvement. In the progressing cases, the intensity of the urochromogen reaction has increased. A persisting positive urochromogen reaction with a tuberculous joint process is sufficient indication for amputation.—*Über die Bedeutung der urochromogen Reaktion für die Prognose der chirurgischen Tuberkulose, Klare, Münch. med. Wchnschr., May 28, 1920, lvii, 635.*

Albumin, Lymphocytes and Tubercle Bacilli in the Sputum.—Takeuchi examined 132 sputa, 77 of which contained tubercle bacilli. The positive and negative groups were both examined for albumin, lymphocytes and eosinophiles. There was a conspicuous difference in the relation of these substances. In the positive group, albumin, a preponderance of lymphocytes and eosinophiles were all found in 71.4 per cent; and albumin, a preponderance of lymphocytes, but no eosinophiles, in 11.4 per cent. Among the negative sputa, which were not necessarily nontuberculous, albumin, lymphocytes and eosinophiles were usually not present. The ratio of instances where albumin, lymphocyytes and eosinophiles were present in the negative group was 9 per cent. The conclusion is drawn that in a sputum which contains albumin, a preponderance of lymphocytes should be suspected to be tuberculous even if tubercle bacilli are absent, and if eosinophiles are present the suspicion is strengthened, as tubercle bacilli, albumin reaction and a preponderance of lymphocytic cells in sputum maintain a parallelism, while eosinophiles go parallel with these three to a certain degree.—*Albumin, Lymphocytic Cells and Tubercle Bacilli in the Sputum, K. Takeuchi, N. York M. J., April 20, 1921, cxiii, 574.*

Tuberculin Reaction During the Menses.—Coulaud presents evidence that the menstrual periods and the menopause represent periods of lessened resistance to tuberculosis, like childbirth. His data also show that these three, parturition, the menopause and the menses, are periods of extra activity on the part of the thyroid. The response to the skin tuberculin test is less pronounced during these periods of energy. This hyperthyroidism can be effectually combated by ovarian treatment, which seems to rest the thyroid. It may likewise exert a favorable influence on the tuberculosis. Jacquerod has reported its success in combating hemoptysis and menstrual fever in the tuberculous. Everything seems to show that intensive functioning of the thyroid body is an important factor in the weakening of acquired immunity. And we know that the thyroid strives to function more to make up for any loss of ovarian functioning.—*La cuti-réaction à la tuberculose pendant les règles et apres ovariotomie, E. Coulaud, Bull. et mém. Soc. méd. d. Hôp., February 17, 1921, xxxvii,* 155.

A New Method of Staining the Tubercle Bacillus.—The method, already employed in Germany during the war under the name of Keurich's method, gives remarkably constant results and is economical of time and reagents. (1) Slow process: (a) stain slides twelve hours in cold Ziehl solution, or five minutes in hot; (b) freely wash in water; (c) plunge slide into a 10 per cent solution of sulphite of soda until completely decolorized; (d) after rapid washing, counterstain in methylene blue. The advantages of the method are a complete decolorization of the slide, and the impossibility of decolorizing the bacilli, even after several hours immersion in the sulphite solution. (2) Rapid process: (a) stain with Ziehl, cold, for 5 or 6 minutes; (b) wash and decolorize with 10 per cent sulphite solution; (c) counterstain with 1 per cent malachite green or with methylene blue. Histological sections may be stained in the same way and the tissues less altered by the sulphite of soda than by the ordinarily used nitric acid. Comparisons made with acid and alcohol decolorization show the method described to be equally satisfactory.—*Une nouvelle méthode de coloration du bacille de Koch, Durupt, Presse méd., January 1, 1921, xxix, 5.*

Tubercle Bacilli in the Blood of Tuberculous Patients.—This question has been dealt with by several investigators. Two methods of investigation have been followed. The first, the microscopic examination of the blood, is open to the objection that the finding of acid-fast bacilli is not proof that they are tubercle bacilli. The second method, that of inoculating the blood into susceptible animals, is the only convincing one. Previous investigations have established that the presence of tubercle bacilli in the blood of tuberculous patients is rare and so capricious in its occurrence, that no rule can be laid down as regards its relation to the various manifestations of tuberculosis. The technique followed by the author consisted in the drawing of 10 cc. of blood from the vein of a patient and inoculating it intraperitoneally into a guinea pig. More than 80 experiments were made. All the pulmonary cases had positive sputum. The surgical cases were such as to leave no doubt as to their nature; they were all undergoing sanatorium treatment and their general condition was fairly good. The following varieties of patients were tested: those with pulmonary lesions and pyrexia, whose blood was taken during the fever or two hours before the onset of fever; those with surgical tuberculosis, without fever and with fever; those with pulmonary tuberculosis without fever; milk of women with tubercle bacilli in their sputum. Out of 84 experiments positive results were obtained in only 10 cases, while 2 were doubtful. These 12 were cases of pulmonary tuberculosis with temperatures varying daily between 97° and 99.5° F. Control experiments were undertaken with the blood of tuberculous patients during pyrexia, to see whether it possessed bactericidal properties. No such evidence was obtained.—*Are Tubercle Bacilli Present in the Blood of Tuberculous Patients? A. Distaso, Tubercle, March, 1921, ii, 251.*

Pleural Effusion on the Healthy Side in Artificial Pneumothorax.—Effusion in an artificial pneumothorax cavity is very frequent but up to the present only two cases have been reported where this occurred in the opposite pleura. Two further cases of this kind are reported in which the patients survived and the pneumothorax treatment could be continued. The following conclusions are drawn: (1) Effusion on the opposite side is an independent complication and is not caused by irritation of the mediastinal pleura. (2) Such effusions are serious but not necessarily fatal. (3) The evolution of such pleurisies is identical with that of ordinary pleurisy. (4) Treatment should be symptomatic.—*Pleurésie exsudative du "côté sain" chez deux malades traités par le pneumothorax artificiel, L. de Reynier and G. Rossel, Rev. méd. de la Suisse Rom., March, 1921, xli, 169.*

Repeated Hemoptysis Caused by a Calculus.—The expulsion of calculi in the sputum is not uncommon and may be accompanied by small haemorrhages. The following case is cited as having particular interest and possibly explaining some cases of repeated hemoptyses: A young woman, who was under observation for about nine years, had repeated hemoptyses in spite of treatment with coagulants, artificial pneumothorax, tuberculin, etc. The lungs showed practically no abnormality, except on the X-ray plate, some enlargement of the left hilum shadow and two small well defined spots. Finally a calculus was expectorated and the X-rays showed the disappearance of one of these spots. After this the hemoptyses ceased. The author believes that this calculus, the result of an old cicatrized tuberculous lesion, was the cause of the hemoptyses in the same way as a foreign body may be.—*Hémoptysies à répétition provoquées par la présence d'un calcul, M. Jaquerod, Rev. méd., de la Suisse Rom., March, 1921, xli, 166.*

The Old and New Conceptions of Scrofula.—Professor Marfan delivered a lecture on this subject last January at the Hospital for Sick Children, Paris, an abstract of which appears in the *Journal de médicine de Paris* of March 20, 1921, xl, 8. The older view of scrofula obtained unmodified until toward 1880, its leading manifestations then comprising enlarged lymph nodes, scrofulous facies, blepharitis, keratitis, otorrhea, fungous disease of the joints, etc. The change was brought about by the introduction of bacteriology, which science soon showed that the majority of these lesions were due to the ordinary pyogenic cocci. The enlarged lymph nodes in the neck were often due to the tubercle bacillus and the tracheobronchial glands were invariably of this origin; there was a tuberculous caries of bone and various tuberculous processes in the skin. But these tuberculous manifestations comprised under the head of scrofula were notably benign, and their presence did not indicate that the subject would be phthisical in after years. On the contrary, the presence of these lesions seemed to predicate a certain amount of natural or acquired immunity to the bacillus. But under the age of five years the cutireaction is positive and violent. Certain obstinate and obscure dermatoses are regarded by some observers as tuberculides while others look upon them as due to pyogenic cocci. The young scrofulous child is very apt to show the association of a slight degree of rickets and this suggests that diet should play an important rôle in the treatment.—*Editorial, Med. Rec., May 14, 1921, xcix, 838.*

Spontaneous Pneumothorax.—Spontaneous pneumothorax, though usually considered as a concomitant of advanced tuberculosis of the lungs, may occur in but slightly or moderately advanced cases. It is a misconception to think that this condition is produced only by ulceration through a cavity wall into the pleural sinus; it may quite as likely be the result of a tear into the lung tissue at the site of a pleuritic adhesion.

This may be brought about by sudden exertion, as coughing or sudden or undue physical effort; a tear results and, with air escaping from the lung, a pneumothorax is produced. Spontaneous pneumothorax occurs occasionally in cases in which an artificial pneumothorax has already been produced; here, ulceration through the thin cavity wall into the pleural cavity makes the case an open one; the accident is usually painless. In all cases of pulmonary tuberculosis, sudden pain after exertion, as coughing or other violent muscular exercise, should immediately challenge the attention of the physician. Again, dyspnea should never be regarded as an ordinary concomitant of pulmonary tuberculosis. Its advent should always be considered as an urgent indication for a complete survey of the chest. Spontaneous pneumothorax is far more common than is usually supposed.—*Spontaneous Pneumothorax, E. A. Gray, J. Am. M. Ass., April 23, 1921, lxxvi, 1147.*

Dental Caries and Tuberculosis.—Paul Ferrier has made the following statements: (1) Demineralization of the bones has a corollary dental demineralization. Both are decalcification. (2) Tuberculosis shows more decalcification than other general diseases. (3) Dental decalcification is found in the tuberculous as well as the pretuberculous, as multiple caries presenting certain clinical peculiarities. In general the tuberculous have less resistant teeth and show more caries than nontuberculous individuals of the same station in life. Lemoine and Jean-Paul Ferrier do not accept this latter statement, but the author criticizes their control cases as these were chosen from a clinic for mouth diseases. His own observations show that 33 per cent of tuberculous patients have dental deficiencies, while controls from medical cases showed only 28 per cent, and from surgical cases 20 per cent. He considers that the state of the teeth furnishes help in prognosis as indicating the calcification of the patient.—*Fréquence comparée de la carie dentaire chez les tuberculeux, P. Fargin-Fayolle, Presse méd., January 15, 1921, xxix, 44.*

Pleuropulmonary Tuberculosis and Chronic Tuberculous Pericarditis.—The patient, a painter twenty-five years of age, came to the hospital January 5, complaining of severe pains in the left chest of several weeks' duration. Cough began in 1918, while the patient was in military service. He had then been treated for five months for right-sided pleurisy. He had since lost about 18 kgm. Family history is negative. Clinical examination reveals slight cyanosis of the lips and extremities; pulse small, 100 to 120 a minute. There is less movement of the right than of the left lung apex, slight impairment of note with increase of resistance in the supra- and infraclavicular fossae, the supra- and infraspinous fossae and the right scapulovertebral space, and rough breathing over the right apex anteriorly and posteriorly. There is a pleural friction rub in the fourth and fifth intercostal spaces anteriorly and to the right. Examination of the heart reveals enormous enlargement, absence of heart impulse, faint heart sounds and pericardial friction rub. On X-ray examination the heart is very large, the outlines irregular, the apex fixed, the pericardium adherent to the diaphragm, the lungs show increased shadow density over the right apex, decreased mobility of the right diaphragm, and marked shadows indicating hilum adenopathy. Pericardial puncture reveals 1 cc. of fluid which was clear at first, later tinged with blood. Cytological examination of this fluid shows red cells and a few small lymphocytes. The absence of an acute infection makes the diagnosis of tuberculous pericarditis probable. Chronic tuberculous pericarditis presents well known clinical and anatomical characteristics. The mediastinum is always involved and there are adhesions between pericardium, pleura and vertebral column. There may be clear fluid or caseous material between the layers of the pericardium. The heart is not always enlarged. There is enlargement of the liver with congestion and more or less sclerosis. Pulmonary, cardiac or hepatic complications supervene. The outcome is always fatal although the evolution of the disease itself may be very slow. The treatment is purely symptomatic.—*Tuberculose pleuro-pulmonaire avec péricardite chronique tuberculeuse, Daco, Liege Méd., February 19, 1921, xiv,* 240.

Tuberculosis of the Heart.—A case is reported in which a tuberculous focus was situated in the wall of the left auricle, and had invaded the mouths of the pulmonary veins, the interauricular septum, and the rings of the auriculoventricular orifices. There were areas of caseation, and tubercle bacilli had been demonstrated. The lesion was apparently primary, and no tuberculosis was found elsewhere in the body. The history was of two months' duration, and the signs during life were those of hypertrophy and dilatation of the heart without murmurs. Of 41 cases of tuberculosis of the heart seen by the author, records showed that only one had so extensive a lesion.—*Reported at Meeting of Section for the Study Disease in Children, Royal Society of Medicine, by Dr. T. H. Gunewardene, Brit. J. Child. Dis., April–June 1920, xvii, 91.*

Dextrocardia Due to Right-Sided Pleuropulmonary Lesion.—Attention has frequently been called to the displacement of the heart towards the right by leftsided pleurisies but little attention has been paid to the pulling of the heart to the right side by sclerosis of the pleura or of the lung. Five cases of dextrocardia from this cause were observed by the authors in less than a year; in two the condition was complete. No especial symptoms were caused by the displacement.—*Dextrocardie acquise par lésion pleuro-pulmonaire droite, Papillon and Flipo, Presse méd., October 9, 1920, xxviii, 716.*

Healed Case of Tuberculosis of the Peritoneum.—A soldier of 21 suffering from tuberculous peritonitis received several tappings and in addition heliotherapy, but every time the abdominal cavity refilled promptly. The patient complained of abdominal distress and diarrhea, had a poor appetite and was continuously bedridden. An exploratory laparotomy revealed numerous nodules all over the peritoneum. Eight days after the operation the abdomen was again filled with fluid. Three more punctures were made at monthly intervals. After the last, the fluid did not return, and the temperature remained normal. Six months later the appetite returned, the bowel movements became normal and the patient was up and about. Thus, a case of tuberculous peritonitis with ascites, where the prognosis had been very grave, was apparently cured by persevering treatment.—*Geheilter Fall von Peritonealtuberkulose, Jentsch, Zentralbl. f. inn. Med., January 22, 1921, xlii, 50.*

Tuberculous Bone and Joint Disease.—Sorrel is chief surgeon of the seashore hospital at Berck, and in his experience the combined heliotherapy and seashore environment form the most energetic treatment at our disposal for tuberculosis of bones and glands. He does not place much value on drugs, and relates that autoinoculation with fluid from the diseased joint has been abandoned for various reasons. Serotherapy has given inconstant results, and has to be kept up a long time to be effectual. These and tuberculin are still on trial, as are also high frequency currents, but roentgen ray treatment of tuberculous glands has already given fine success in certain cases. With bone disease, although general treatment is of first importance, local measures must not be forgotten. They vary, however, with the age; in children the minimum of intervention should be the rule; in adults, resection. After the age of fifty, a cure cannot be counted on, and amputation is generally called for. We thus have quite an array of measures at our disposal but we cannot claim to shorten very much the duration of a tuberculous lesion. It runs an almost cyclic course. We cannot cure it in six months or a year, but at least we can guide it, reducing the destruction, and providing for healing with minimum of loss of function. In the differential diagnosis, the effusion may show the presence of lipolytic ferments and predominance of lymphocytes. Cultivation of the pus is generally regarded as giving unreliable findings.—*Quelques généralités sur le diagnostic et le traitement des tuberculoses osteo-articulaires, E. Sorrel, Presse méd., February 5, 1921, xxix, 101.*

Tuberculous Disease of the Hip Joint.—Next to tuberculous disease of the spine in children tuberculous coxitis takes second place as the most common and most important affection of the joints. In one series of 1000 cases reported by Whitman, over 88 per cent were in children under ten years of age. The disease runs such a slow course that many of the classical symptoms are not evident until long after the tuberculous focus has become deeply fixed in the hip joint area. There is perhaps not a disease more easily recognized and yet it is very frequently treated for rheumatism. Possibly the child had been complaining for some time of pain in the region of the knee, or there may have been a limp and stiffness of the leg, particularly in the morning. The child very likely had been sleeping restlessly, crying out at night as if in pain; or tires easily and stops frequently in its play to rest; and in the resting attitude the affected limb is favored. In the early stages the well foot of the normal side would be placed below the other foot, in order to fix the leg, and prevent motion of the hip. Later the well foot would be placed so as to secure extension of the leg that hurt. The leg of the affected side would be found to be in abduction with flexion at the thigh, the position of protection. Attempts to flex the thigh on the abdomen would be resisted. These motions could be done under a few whiffs of chloroform, for then the muscle spasm would be relaxed, the pain relieved and the irritation stopped. The X-ray is an indispensable ally. The most usual sites of erosion are seen at the point of impact between the upper margin at the head of the femur and the corresponding portion of the acetabular rim. Relief can be given these patients by application of a well fitting cast if seen early. The process of treatment from cast to brace, and crutch and weight bearing, finally to both feet on the ground and walking without support occupies from one to two years' time.—*Tubercular Disease of the Hip Joint; an Appeal for Earlier Diagnosis and Treatment, J. D. Trawick, Kentucky M. J., March, 1921, xix,* 127.

Mastoiditis and Suboccipital Pott's Disease.—Portmann of Bordeaux contributed a monographic article on the above named subject in the *Revue de Chirurgie* for September-October, 1919, xxxviii, 9–10. The subject is on the border line between surgery and otorhinolaryngology. The author finds that the question of differential diagnosis between the two above named affections has been much neglected. Failure to make the correct diagnosis might in either mistake prove disastrous. Suboccipital Pott's has repeatedly been diagnosticated as mastoiditis, but the medical men who make the mistakes do not always publish them. Moure of Bordeaux has seen two cases and the present author one, which is described. The differential diagnosis applies to three separate conditions: (1) An abscess has not formed; (2) there is a cervical abscess; (3) there is a fistulous tract. If there is no abscess forming as yet, auricular symptoms point to mastoid disease and absence of such symptoms to Pott's. Stiff neck in mastoiditis is usually absent or at best very slight, while it is a marked symptom of Pott's disease. In Pott's the mastoid region shows no deformation. Pain, both spontaneous and induced, is referred to the affected region. After abscess formation has occurred, the pain in Pott's is not conspicuous, while in mastoiditis it is pronounced and unilateral. In Pott's we have a "cold," in mastoiditis a "hot" abscess. Punctates show the characters of the two types. If not seen until the fistulous stage the fistula presents the characters of tuberculosis in the Pott's patient and that of a phlegmon in the other. Both the radiograph and the probe should be decisive.—*Editorial, Med. Rec., March 12, 1921, xcix, 443.*

Primary Tuberculosis of the Testicle.—Tuberculosis of the body of the testicle as a primary focus in the human economy is extremely rare. It occurred experimentally in 2 rabbits out of 28 receiving an injection of tubercle bacilli directly into the aorta. Critical review of all available literature does not reveal a substantiated clinical case. The case reported here bears out this contention. The patient, age thirty-one, married four years, had gonorrhea fourteen years previously, complicated by acute left epididymitis, but recovered completely after seven weeks. Eight years ago the patient was kicked in the right testicle during a football game. No swelling or after effects were noted. In February, 1920, the patient noticed a slow enlargement of the left testicle which became tender about March 25. The author saw the patient for the first time on April 3, and found slight hydrocele with marked involvement of the body of the testicle and with a small nodule on the body proper, without evidence of any involvement of epididymis or vas. The patient was well nourished and physical examination as well as urine, blood and chest X-ray examination were negative. Orchidectomy was performed. The laboratory reported diffuse tuberculosis of the testicle with no involvement of the epididymis. A second report stated the same. Serial sections of the epididymis were then insisted upon and revealed a small single tubercle about 4 mm. in diameter. The author has come to the conclusion that in the vast majority of cases primary tuberculous involvement of the genital tract is an ascending process.—*Primary Tuberculosis of the Body of the Testicle, E. G. Mark, J. Urol., February, 1921, v,* 171.*

Association of Tuberculous Meningitis with Meningococci and Parameningococci.—Tuberculous meningitis can develop in association with other infections. The association of the Koch bacillus with meningococci is frequent, according to certain authors, but a certain number of reported cases require confirmation. An exact diagnosis can be arrived at only by examination of the cerebrospinal fluid. Such diagnosis is practicable in the living subject, and should be employed in all cases. The meningococcus infection antedates the other. The prognosis is fatal.—*Association de la méningite tuberculeuse et méningo- ou paraméningococcique, Barthas. Thèse de Toulouse, July, 1920, 95, from Arch. de Méd. des Enfants, February, 1921. xxiv, 132.*

Tuberculosis of Goats.—On the basis of the assumption that the goat is rarely tuberculous, the substitution of goat's milk for cow's milk has been extensively made as a prophylactic measure against human tuberculosis. The fact is that tuberculosis in goats is not nearly so rare as has been thought, and the false security felt by those using goat's milk because of the belief that there is no possibility of the transmission of the disease is a dangerous thing. It is admitted that tuberculosis is far less prevalent among goats than among cattle. Nevertheless its occurrence must be recognized and a warning should be sounded, and physicians who have recommended the use of goat's milk as wholly free from tuberculous infection should bear in mind the possibility of the transmission of the disease through this agent. A review of the foreign literature shows that in inspected abattoirs recognition of the disease is not uncommon.—*Tuberculosis of Goats, C. Murray, S. H. McNutt and P. Purwin, J. Am. Vet. M. Ass., April, 1921, lix, 82.*

Tuberculosis in Milk Goats.—An imported herd of Saanen and Toggenburg goats which arrived from Switzerland March 3, 1920, was recently found badly infected with tuberculosis on a farm in the vicinity of Leeds, Iowa. The trip to the quarantine station at Athenia, N. J., consumed about five months. After a quarantine of about eighty-five days the animals arrived at their destination at Leeds, the trip being made by express. As two goats which were in a diseased condition failed to respond to treatment by the local veterinarian, they were shipped to the Experiment Station at Ames, Iowa. Dr. Murray reported the finding of tuberculous lesions in one of the goats on postmortem examination. On November 30, 1920, the writer applied the intracutaneous tuberculin test to the herd, which included 33 imported does, 8 imported bucks and 1 native doe. Seventy-two hours later observations revealed 6 well marked positive reactors. On December 6, an ophthalmic disc was instilled into the left eye of each goat. At 8 P.M., December 8, all goats with the exception of bucks and the native doe were given subcutaneous injections of tuberculin. On December 9, at 8 P.M., a second ophthalmic disc was instilled into the left eye of each goat. Observations were made three hours later and continued hourly until 3 P.M. the next day. One goat has died in the meantime. All six goats which had previously reacted to the intracutaneous test gave a positive reaction to the ophthalmic test. Three of the 6 reactors to the ophthalmic and intracutaneous tests gave a positive reaction (thermal) to the subcutaneous test. Two showed a decided rise of temperature. One died seven hours after the injection, with subnormal temperature, and revealed at autopsy extensive caseocalcareous lesions in the bronchial and mediastinal lymph nodes and in the lungs. Smears from the lesion showed acidfast bacilli and inoculations into guinea pigs produced tuberculosis. On December 24, autopsies were made on 4 reactor goats, and well marked tuberculous lesions were found. The original source of this infection has not been ascertained. The safest method to prevent the spread of tuberculosis to the human family from this source would be either to pasteurize the milk or to test the goats with tuberculin and remove reactors. Goats may be badly affected with tuberculosis and still appear in good physical condition, as was the case in this herd.—*Tuberculosis in Milk Goats, G. E. Golden, J. Am. Vet. Med. Ass., April, 1921. lix, 79.*

Tuberculosis Eradication Among Cattle in Pennsylvania.—There are approximately 1,000,000 dairy and breeding cattle on 202,298 farms in Pennsylvania. On 85,000 of these farms there are approximately 100,000 tuberculous animals. As the result of the first herd test 9 per cent of all the cattle tested were condemned. The problem is a large one. It is gratifying to know that the disease can not only be controlled, but actually eradicated from infected herds, in a comparatively short time, and once freed they will remain so. By testing and retesting free and infected herds, a very good idea as to the value of the subcutanous test was obtained. In retesting free herds the subcutaneous test had an efficiency of 98 per cent. One of two things, or both, happened to account for the 2 per cent inefficiency. The animals which reacted on the second test, after having successfully passed the first test, either became infected between the two tests or they escaped the first test. If we can obtain as good results with the intracutaneous as we are now obtaining with the subcutaneous test then the former will be adopted as a single official test. Infected herds can be freed from tuberculosis by two tuberculin tests with few exceptions: (1) by careful application and interpretation of the tuberculin tests, (2) by prompt removal of the infected animals, (3) by a thorough cleaning and disinfecting of the premises, (4) by immediate improvement of sanitation, if faulty, and (5) by not feeding calves on milk from doubtful sources, unless properly pasteurized. Accredited herds will continue to remain accredited, if owners will comply with the following: (1) by correcting sanitation, if faulty, (2) by cleaning and disinfecting stables, etc., at least once a year, (3) by guarding the herd against exposure from a neighbor's herd, providing the health of the latter has not been determined; (4) by feeding calves pasteurized milk, unless the milk is from tested animals, (5) by using extreme care in adding new animals and (6) by keeping cattle separate and apart from cattle of herds not under supervision, if shown on exhibition.—*Progress of Tuberculosis Eradication in Pennsylvania, S. E. Bruner, J. Am. Vet. Med. Ass., April, 1921, lix, 32.*

Complement Fixation in Bovine Tuberculosis.—The antigen of Besredka fixes alexin in the presence of serum of tuberculous cattle. In the sera of 304 known tuberculous cases, 84.5 per cent positive reactions were recorded. Of 90 sera where tuberculosis was not demonstrable at necropsy, 2.2 per cent reacted positively. Where tuberculosis was not advanced (glandular only) the percentage of positive reactions was 60 per cent. Where the involvement included lungs, pleura, peritoneum and some of the abdominal viscera, the reaction was 85 to 95 per cent positive, and when the disease was generalized all sera reacted positively. The method should be an important diagnostic aid in bovine tuberculosis.—*Le diagnostic de la tuberculose chez les bovidés au moyen de l'antigène de Besredka, C. Hruska and W. Pfenninger, Ann. de l'Inst. Pasteur, January, 1921, xxxv, 96.*

Excretion of Tubercle Bacilli in Bile.—Marchisotti found the liver often affected in tuberculous cattle. Healthy milk can thus become readily contaminated by droppings from tuberculous cattle, or the apparently healthy cow herself may be voiding tubercle bacilli in bile by way of the stools. His research was done on cattle slaughtered for the market and thus supposedly healthy, the tuberculous lesions being a necropsy surprise. Human urine and stools are liable to transmit the tubercle bacilli as readily as sputum. Tuberculosis of the liver should be classed as open tuberculosis on this account. Tuberculin tests do not reveal the involvement of the liver in particular.—*Excreción de bacillo de Koch por la bilis, A. C. Marchisotti, Semana Méd., January 13, 1921, xxviii, 37.*

Tuberculosis in Small Rodents.—The experiments reported confirm the statements of previous authors, such as A. Koch, Rabinowitsch, De Jong, Weber, Bofinger, Straus, Romer, and A. S. and F. Griffith, that white rats and mice are susceptible to infection with tubercle bacilli, human, bovine and avian types, but are so resistant to small doses that they cannot replace the guinea pig or rabbit in experimental work. Intraperitoneal inoculation of 1 to 2 mgm. offers the surest means of producing infection, which is manifested chiefly by the formation of tubercles in the lungs, and by the intense multiplication of bacilli in the liver and spleen. Intracutaneous inoculation in the ball of the foot occasionally provokes extensive, severe lesions. Infection is favored in general by the introduction of repeated small doses. Only rarely is tuberculous infection fatal to rats and mice. The three types are of about equal virulence. Inoculation of the bacillus of Arloing and bacilli of the piscine types does not cause infection. Infected animals are not very susceptible to tuberculin. The phenomenon of Koch is not observed.—*Contribution a l'étude de l'infection tuberculeuse chez les petits rongeurs, A. Boquet and L. Nègre, Ann. de l'inst. Pasteur, February, 1921, xxxv, 142.*

Pulmonary Botryomycosis.—Botryomycosis is best known to veterinarians as pedunculated fibrous granuloma of horses. The growth usually arises in connection with skin surfaces. In the first case described by Bollinger in 1870 the lung of a horse was the seat of the disease. Although human cases have been reported from France, Italy and Switzerland, it has been observed most commonly in northern Africa and in Morocco. The gross lesions consist of abundant chronic granulation tissue which on microscopic examination reveals granules made up of coccus like organisms embedded in and surrounded by a hyaline matrix. Two views are held in regard to the organism, many regarding it as the usual staphylococcus aureus, others as a specific coccus. Special interest attaches to the case here reported because of its occurrence in the same community from which a previous one with localization in an internal organ was reported. A male infant, four months of age, was admitted to the St. Louis Children's Hospital, September 15, 1920. Nothing in the family history indicated the source of the infection. The baby had always had a hacking cough which had been much worse during the past six weeks. About three weeks before it had a high fever which continued for one week. Clinical examination revealed a temperature of 99.2° F., respirations 50, impaired percussion note over the entire right side, suppressed sibreath sounds and fine crackling râles, and leucocytosis of 20,000 with 62 per cent eosinophiles. The Pirquet test was repeatedly negative. The child continued to grow worse and died October 8. At autopsy there were found centimetre areas of a dark bluish color, most of which were in the posterior portions of the right lung. Histological examination of these areas revealed the presence of giant cells of the type seen in tubercles and of peculiar dark masses which consisted of Gram positive coccoid organisms embedded in a hyaline, eosin-staining matrix. The other organs showed nothing of importance. Cultures on blood agar plates made from the bronchial exudate gave a heavy growth of Gram positive cocci which presented the usual appearance of staphyloocccus albus. With the pulmonary symptoms predominant at the beginning of the disease and persisting for several weeks in such a manner as to suggest pulmonary tuberculosis, one is led to think that this case was a primary bronchopneumonia which terminated fatally.—*Pulmonary Botryomycosis, F. A. McJunkin, Arch. Int. Med., April, 1921, xxvii, 457.*

Prognosis and Antecedent Tuberculosis of Ancestors or Patients Themselves.—Whether a tuberculous ancestry renders a patient more likely to develop a slow chronic form of the disease than would another without such heredity, or whether such a tuberculous ancestry is unfavorable, is still a debated question among clinicians and authors. The influence of a mild childhood infection, as scrofula, tuberculous glands, etc., on the course of a tuberculosis developing in later life must also be studied. The present article reviews some statistics compiled from observations on German and Austrian soldiers who took part in the war, and in whom pulmonary tuberculosis frequently assumed a severe form and rapid course. The author sums up the evidence by saying that the prognosis in pulmonary tuberculosis is, in general, more severe if the patients are individuals stricken down when in perfect health without having been previously, in their childhood, exposed to more or less repeated infections. Ordinarily, it will be less grave in individuals of tuberculous parentage as these have for the most part received such infections and carry the scars of them. It will be most favorable in those who have already had slight manifest tuberculosis.—*Le prognostic général de la tuberculose pulmonaire et les antécédents tuberculeux des ascendants ou des malades eux-mêmes, E. Arnould, Presse méd., January 19, 1921, xxix, 54.*

Tuberculosis and Experimental Endothelial Leucocytosis.—A reaction in the peripheral blood of the guinea pig, similar to the one seen during the last two or three weeks of the usual guinea pig tuberculosis, may be produced by injections of large quantities of killed cultures of smegma, timothy-hay or nonvirulent tubercle bacilli. Although the amounts necessary to produce the reaction approach the lethal dose and the animals in which the leucocytosis is maintained suffer a loss of weight, those injected with smegma or timothy-hay bacillus suspensions succumb no more readily to infection with virulent tubercle bacilli than do the control animals. Grossly and microscopically the lesions in the animals receiving injections of B. phlei and B. smegmatis differ from those of the controls living the same number of days, in that the spleen is small and that the necrosis in the leucocytic foci in the spleen and other organs is slight or absent. Smears from the omentum and other organs of the treated animals show numerous tubercle bacilli and there is every evidence of their being extensively infected. There is little reason to think that the guinea pig offers any resistance to the growth of tubercle bacilli during the first ten days or two weeks of the infection before the tuberculin test becomes positive, so that any beneficial effect from stimulation of the leucocyte which reacts to the greatest degree in tuberculosis would have to be initiated after this time. Injections of suspensions of smegma and timothy bacilli unquestionably influence the gross and microscopic character of the lesions, provided doses large enough to maintain the endothelial leucocytosis are given. Injections of nonvirulent cultures of the tubercle bacillus appear to shorten somewhat the duration of the disease.—*Tuberculosis in Guinea Pigs with an Experimentally Produced Endothelial Leukocytosis, F. A. McJunkin, J. Med. Research, November, 1920–January, 1921, xlii, 201.*

Resistance to Tuberculosis.—The authors believe that carbon dioxide may play a significant rôle in the resistance to tuberculosis. Three per cent carbon dioxide inhibits the growth of tubercle bacilli in the test tube, and 15 per cent is tuberculocidal. Cultures of tubercle bacilli buried in the tissues of animals and permitted to acquire the carbon dioxide concentration of the body are definitely inhibited in their growth, while other cultures, similarly buried, except that ingress of atmospheric air is permitted, show no inhibition. This reopens the consideration of the influence of fatigue, exhaustion, exposure, metabolic diseases, etc., as probably etiologic factors in the causation of tuberculosis in view of their ability to alter the carbon dioxide content of the body.—*Resistance to Tuberculosis: A Nonimmunologic Chemical Factor Worthy of Consideration, H. J. Corper, H. Gauss and O. B. Rensch, J. Am. M. Ass., April 30, 1921, lxxvi, 1216.*

Psychology of the Tuberculous.—Several well known phthisiologists have taught that the tuberculous subject tends to be self-centered and indifferent to the comfort and welfare of others, while Dr. Knopf of New York has expressed his disbelief in this teaching, perhaps regarding the consumptive as as much of an altruist as a patient with any other chronic incurable disease. In a paper on the psychology of the chronic invalid Ichok (*Journal de médicine de Paris* for January 10, 1921, xl, 1) touches incidentally on the psyche of the consumptive. He quotes a page from Daremberg, a famous phthisiologist, on the latter subject, but thinks it would apply with equal force to the sufferer from any other chronic malady. Daremberg attributes strong egoism to the consumptive and narrates a number of its expressions, one being that the victim of this disease cheerfully allows his friends and relatives to wear themselves out in his service and is utterly indifferent to the possibility of communicating his disease to others. Laignel-Lavastine, the well known alienist, speaks of this egoism as negative rather than positive. Realizing his weakness and helplessness, the consumptive accepts attentions as might for the same reason a child. But he does not exhibit an active, aggressive egoism. Ichok barely mentions the characteristic optimism of the consumptive: for if the latter believes that he is getting better—as he is very apt to do—such belief must react on the psyche, and hence perhaps the subject of the *spes phthisica* merely feels that he can make up the sacrifices of his relatives after his recovery. Many adolescents impose on their parents and companions from the same motive—they expect to prosper amazingly in life and then it will be a mere bagatelle to repay favors. The author mentions the surprising sexual potency of many consumptives—amounting at times to an erotomania—and believes that the phenomenon may be in part responsible for the optimistic tendency, since a man who is sexually strong cannot well visualize himself as doomed to death,—*Editorial, Med. Rec., March 26, xcix, 529.*

Value of Artificial Pneumothorax Treatment.—Artificial pneumothorax is limited to patients with unilateral lesions, or to those in whom the tuberculous process on the other side is quiescent. This restricts its usefulness, for hardly more than 3 per cent of all tuberculous patients fall within this category. The great frequency of adhesions forms one of the greatest hindrances to successful treatment. Physical signs and fluoroscopy will not always give assurance whether or not collapse of the lung is possible. In many cases all efforts to enter the pleural cavity are unavailing, although no difficulty is expected. On the other hand, one is often successful on occasions when least expected. Repeated attempts are often necessary before gas can be admitted to the pleural cavity. From an experience during the last six years at the Montefiore Hospital the author confesses frankly that a positive cure is only rarely accomplished. In the majority of successful treatments there is distinct temporary relief, the ravages of the disease are checked for a while, the temperature drops, the cough lessens, and the patient gains weight and is a good deal happier and more comfortable. After a varying interval of improvement there arises some disastrous complications which put a stop to further progress, and the disease pursues its former course. Again, the treatment may induce a longer arrest of the activity of the tuberculous process and give the subject a year or two of comparative comfort. These gains, small as they may seem when compared to the ideal of saving life, are not to be scorned; and where we succeed in attaining them we may justly consider the treatment a valuable therapeutic agent. By keeping in mind the great frequency of complications we must never employ this mode of therapy in early cases, for in them complications are no less common.—*The Value of Pneumothorax Treatment of Pulmonary Tuberculosis, E. P. Boas, N. York M. J., April 6, 1921, cxiii, 517.*

Artificial Pneumothorax in Pulmonary Tuberculosis.—Out of 80 patients on whom artificial pneumothorax was used, Crocket had successful results in 12, partially successful results in 30 and 38 failures. The causes of the limited success he classifies as follows: (1) Adhesions preventing complete collapse, in 9 cases. (2) Extensive disease in both lungs, leading to increased cyanosis and dyspnea, 5 cases. (3) Bronchitis affecting the good lung and recurring from time to time when weather conditions were unfavorable, in 4 cases. (4) Onset of influenza causing extension of the disease in the good lung, in 3 cases. (5) Stopping the injections at too early a period, and reinductions being impossible on account of adhesions, in 2 cases. (6) Patient refusing further injections, having had a fright by the onset of surgical emphysema, one case. Crocket is a firm believer in this method of treatment in suitable cases.—*Artificial Pneumothorax in Pulmonary Tuberculosis. Crocket, Edinb. M. J., August, 1920, xxv, 113.*

Cerium Salts in the Treatment of Chronic Tuberculosis.—Cerium salts modify the cultural characteristics of the tubercle bacillus in vitro and produce a mononuclear leucocytosis in the rabbit and guinea pig. When used for treatment they have a general and a local action. Whenever possible it is best to apply the drug directly to the ulcerations of the skin or inject it into a cavity. But general treatment gives the better results. Intravenously a 2 per cent solution of didymium sulphate is used in doses of 0.08 to 0.1 gm. daily; subcutaneously or intramuscularly, 2 cc. of a 2 per mille lipoid solution are given daily. Renon administers the drugs in addition by mouth, by rectal instillation and by intratracheal injection. Unless the therapy is maintained for a sufficiently long period and given at suitable intervals it is useless. Twenty injections are given daily or on alternate days followed by a rest period of twenty days. In general the treatment is applicable and indicated in chronic tuberculosis and contraindicated in acute or febrile cases. It has been used to advantage in tuberculosis of the lungs, lymph nodes, skin, pharynx and larynx, bones and joints, peritoneum, testicles, epididymis and kidneys. During the first few days of the treatment there is a slight exacerbation of such symptoms as cough, expectoration, suppuration, etc. This is followed by a rapid return to the initial condition; then slowly, step by step, the moisture subsides, suppuration is diminished, the sputum becomes less, the lesions become dry, and finally cicatrization results. Improvement is always slow and progressive, never abrupt and sudden. Frequently the bacilli disappear from the sputum after two or three series of injections. These patients may stop coughing, and have only a trifling expectoration. They can work without fatigue and without elevation of temperature and their physical symptoms subside. Even in the more advanced cases improvement is such that the patients frequently can return to their work. Rapid cures have been observed in lupus erythematosus and rapid improvement in adenitis. Tuberculosis verrucosa subsides. Lupus is often more resistant but several cures have been obtained. —*Technique, indications et résultats du traitement des tuberculoses chroniques par les sulfates de terres cériques, H. Grenet and H. Drouin, Presse méd., February 23, 1921, xxix,* 153.

Calcium in Pulmonary Tuberculosis.—Prest has been giving calcium lactate to a majority of the 94 patients in the Ayrshire Sanatorium and is convinced of the benefit it produces. In many girls and young women and in some women at the menopause, who are also tuberculous, one of the distressing symptoms is menorrhagia. This condition can almost invariably be benefited by the administration of calcium. Calcium largely ceases to be excreted during pregnancy, the retained calcium being used up by the growing foetus. During lactation calcium is largely secreted in the milk. This is probably the chief reason why lactation has such an injurious effect on tuberculous women. The effects observed during the administration of calcium are fall in temperature, cessation of night sweats, increase of energy, cessation of menorrhagia, retrogressive changes in the lesion and improvement of coexisting anemia. The drug was usually given as a powder of 15 grains of the lactate every night during alternate weeks. —*Calcium in the Treatment of Pulmonary Tuberculosis, E. E. Prest, Brit. M. J., March 19, 1921, no. 3142, 420.*

Calcium and Tuberculosis in Rabbits.—Massini injected young rabbits with calcium chloride after they had been inoculated with tuberculosis, and found that they lived a little longer than the controls.—*Calcium und Tuberkulose beim Kaninchen, R. Massini, Schweiz. med. Wchnschr., March 10, 1921, li, 233.*

X-ray Treatment of Tuberculous Laryngitis.—Few reports have been made on the X-ray treatment of tuberculosis of the larynx but a few isolated instances have been encouraging. Seven cases are reported here and 10 others have been treated. The exposures are made every eight to ten days, alternating from the front to either side, using 16 to 20 X, according to Kienböck, through the skin to the larynx. The induction apparatus of Siemens and Halske, and Müller's tubes are used with a current of three and a half milliamperes and a three mm. aluminum filter. The period of exposure and the intervals vary with the reactions. Daily spraying of the larynx with menthol is also employed. No harm was ever noted. The infiltrative cases seem to give best results. Ulcerations do not respond so well. Local reactions, such as swelling, with increased cough and expectoration and a feeling of dryness, were regularly noted. They usually lasted only one day. An objection is that the treatment must be carried out over a rather prolonged period of time. The routine rest treatment is continued.—*Zur Röntgenbestrahlung der Kehlkopftuberkulose, J. Fleck, Beitr. z. Klin. d. Tuberk., November, 1920, xlv, 268.*

Heliotherapy in the Alps.—Different parts of the continent show variations in the quantity and quality of light which reach the earth's surface. This may affect the cure in different locations. Nevertheless sunlight treatment can be carried out anywhere where sufficient sun is available. The rays stimulate and are beneficial to tissue cells. They are however very toxic for bacteria, especially tubercle bacilli. Sunlight stimulated the proliferation of cells that had not been destroyed, whereas for cells damaged beyond repair the rate of disintegration was increased. Conditions of defective metabolism, anemia and rickets are well suited for sunlight treatment. Sluggishly healing superficial wounds such as varicose ulcers also promptly respond to the stimulation.—*Heliotherapy in the High Alps, A. Rollier, Lancet, March 19, 1921, 582.*

Effect of Ultraviolet Radiation on Vitamines.—Eight hours of continuous application of ultraviolet radiation to fat-soluble vitamines destroyed them, whereas there was no effect upon the water-soluble ones. Since the former are considered to be important factors for growth, and inasmuch as the mercury quartz light has been employed for sterilization of milk, the evidence points against such use of these radiations.—*Action des rayons ultraviolets sur les vitamines, S. Zilva, La Nature, May 15, 1920, no. 2405.*

Action of the Visible Light Rays on the Body Temperature.—Exposure to infrared rays elevates the temperature at the surface to 3.2°C. over that of the depths. With the visible rays the reverse occurs, that at the depths being higher than that at the surface by 1.6°C. Further exposures of guinea pigs made at the Finsen Institute verified the above findings; but here the temperature of the body, under the action of the visible rays, was three degrees higher than that at the surface. With the ultrared rays blisters easily developed on the backs of the guinea pigs (that had been shaved) after thirty minutes' exposure. Visible rays never cause this.—*Action of Visible Rays on Temperature, C. Sonne, Hospitalstidende, January 5, 1921, lxiv*, i.

Institutions for Sun Treatment.—A perfect heliotherapeutic institution with excellent results may be obtained with easily improvised arrangements. Certain conditions should be fulfilled regarding climate, situation and management. The place should admit as much sunlight as possible and the air should be bracing. In mountainous countries, such as Switzerland, a high altitude fulfills these requirements. The ideal height is 3000 to 5000 feet. Leysin is 4400 feet high, sheltered from the north wind and enjoys the sun for a large number of hours during each day. Three principal types of building are described. The first of these is a mountain chalet converted into a sanatorium. On the south side wide balconies were constructed on to which the patients' beds could be wheeled. The children's house and its annex were provided with large balconies placed on the front of the house in such a way as to be exposed to the sun's rays during almost the whole day. The second type, a mountain hotel converted into a sanatorium, was originally a tourist hotel built in a magnificent situation 5000 feet above sea level. The third type is a sanatorium constructed and arranged entirely with a view to the practice of heliotherapy. This building consist of a central block and two large wings. The central block contains on the ground floor the consulting room, roentgen departments, rooms for orthopedic and phototherapy, bacteriological laboratory and offices. On the first floor are dining room, billiard and smoking rooms and kitchens, and on the fourth floor a surgical dressing room and operating theatre for nontuberculous infections. The balconies of the left wing are used for the sun cure. The first floor balconies of the right wing are reserved for children. A solarium on the roof is ideal for the suncure, as a playground, and for patients who are making their first attempts at walking. It is important that the balconies are exactly on a level with the dormitories so that the patients may be wheeled everywhere in their beds without jolting. The beds must be high and should be fitted with large and solid wheels, and the mattresses should be hard, so that there is no danger of the patients assuming a bad posture. In certain cases special apparatus is used for immobilizing patients, especially children with spinal caries or hip disease. These devices are very simple, and they can be opened and closed at will and cannot interfere with the suncure. The suncure is the most perfect fulfilment of the demands of orthopedic and conservative surgery, since it sends back to their work individuals with limbs and articulations intact in almost every case. Tuberculous foci which have opened spontaneously or which have been incised are much slower and more troublesome in healing than closed lesions. Gradual increase in the duration of the sun baths must be made to suit individual cases. The amount of exposure must be reduced or temporarily interrupted on the least sign of intolerance, as rise of temperature or pulse, general malaise, erythema, etc. Exposures should last only a few minutes at the start; as soon as the skin is pigmented two or three hours a day may be undergone without danger. The head and nape of the neck should always be protected by a white cotton hat. This method has never resulted in accidents at Leysin. Afebrile cases of pulmonary tuberculosis are greatly benefited by the treatment. Chest and back can be exposed only after the patient has been accustomed to exposure of the legs, the thighs and the abdomen. Among the accessories of heliotherapy the work cure has yielded the most remarkable results. When strictly supervised it constitutes a therapeutic factor of prime importance. Heliotherapy has an important part in preventive medicine. With this object in view an open air school was started near Leysin for predisposed children and to form a half-way house to prepare convalescents for their return to life on the plains. These schools should be established universally in towns and villages. —*The Construction of an Institution for the Heliotherapeutic Treatment of Surgical Tuberculosis, A. Rollier, Tubercle, March, 1921, ii, 241.*

Treatment of Pulmonary Tuberculosis with Partial Antigens. —In order to test properly and with any degree of throoughness a remedy for which its discoverers, on the basis of long and extended experience, have set up pronounced therapeutic claims, four requirements must be complied with: The examiner must be familiar with the method of using the remedy, and test it long enough. Ott used the partial antigens from February, 1914, until into 1917, not only in ambulant treatment but also in hospitals. The number of patients must be sufficiently large to elminate as far as possible the element of chance, which plays a part in all disease. Ott can report on at least 489 cases of pulmonary tuberculosis. Finally, the remedy must be tested impartially and with interest, otherwise it is easy to bring any remedy into discredit by selecting hopeless cases. For purposes of comparison, he gives the result in 420 practically corresponding cases formerly treated by him with old tuberculin. The results are essentially the same as with the partial antigens. Ott concludes that the Deycke-Much partial antigens are by no means entirely innocuous. In their therapeutic effects they are not in the least superior to tuberculin. The theoretic premises of the treatment rest on a very uncertain basis.—*Sechsjäherige Erfahrungen in der Behandlung der Lungentuberkulose mit den Partialantigenen nach Deycke-Much, A. Ott, Münch. med. Wchnschr., October 1, 1920, lxvii, 1139.*

The Friedmann Treatment.—The chief characteristic of the method is the inoculation of living acid-fast bacilli, isolated from a turtle. They are differentiated from human tubercle bacilli (1) by growing at a temperature between 13° and 42°C., (2) by producing miliary tuberculosis in cold-blooded animals, and (3) by being harmless for warmblooded animals. Friedmann would classify them as a separate species, intermediate between the human and reptilian bacilli. Pierkowski and others dispute this claim, saying that they are human bacilli, accidentally infecting the turtle and becoming transformed gradually in its new host. Calmette states that Friedmann's cultures contain human as well as turtle bacilli. Friedmann maintains that his bacillus, while innocuous for man, will immunize against human and bovine infection, and supports his claim by animal experiment, but in 1912 he was more conservative than in 1904. Orth and Ehrlich could not confirm Friedmann's claims. Selter in a recent work was unable to prove the existence of antibodies following inoculation with the Friedmann organism and could not alter the course of disease in guinea pigs infected with human organisms by treatment with turtle bacilli. Friedmann has inoculated infants and caused positive skin reactions which later disappeared, but Selter in duplicating this work obtained negative results. Clinically, the method has been tried in surgical cases with contradictory results and no definite conclusions can be drawn at present. With pulmonary tuberculosis the results are also inconclusive and accidents have been reported from the use of this method. Some successes have been obtained, whether due to the method or not is a question, and most results are negative or doubtful and cases as comparable as possible have given different results. The writer concludes that Friedmann's case is far from being proved and time alone will decide. All new methods have produced transitory successes.—*À propos du traitement de la tuberculose par la méthode de Friedmann, M. Nathan, Presse méd., November 13, 1920, xxviii, 819.*

Treatment of Surgical Tuberculosis.—Among 4600 cases, there were 350 cases of joint tuberculosis, about 7 per cent. Of these cases 253 were treated: 28 operatively and 225 conservatively. The first thing that deserves warmest advocacy is the securing of all facilities necessary to carry out general treatment, especially that of heliotherapy and outdoor life. Barring a few patients in especially favorable circumstances this should mean institutional treatment for the majority of cases. Severe cases of either Pott's or hip or shoulder disease will do better in recumbency than in ambulatory treatment and the general trend should be more toward prolongation of recumbency. While the division of indications into conservative and operative treatment largely parallels the division into adult and juvenile tuberculosis, there are operative indications for radical interference in children, which, if undertaken at all, should be done at an early time. The best results are obtained by a long period of institutional care so that both recumbent and general hygienic treatment may be administered thoroughly and systematically.—*Operative and Nonoperative Indications in Surgical Tuberculosis, A. Steindler, Iowa State Med. Soc. J., February 15, 1921, xl, 33.*

Climate in Tuberculosis.—The superiority of one locality over another as a place for the treatment of tuberculosis is individual rather than general and the fact that some patients do better in a particular climate or locality is no criterion that a majority of the tuberculous will do equally well there. There is no specific climate for the treatment of tuberculosis. Although many patients are greatly improved by a change of climate, the improvement can be attributed to the effect of change rather than to the virtues of the particular climate. Proper care, which means proper rest, good food and open air, and competent medical supervision, is of much greater importance than climate. Competent medical supervision includes proper medical and surgical treatment for symptoms and complications. Heliotherapy or artificial light therapy may be added to these four well known and thoroughly proved essentials. No acutely ill patients should be sent a long distance. No patient with insufficient funds, irrespective of his physical condition, should be sent to a tuberculosis resort, unless he can enter an institution. A patient with sufficient funds should not be sent away unless he can and will place himself under proper medical supervision and follow instructions absolutely. A change is indicated in a chronic case, which has reached the point where the condition remains stationary after a sufficient length of time, providing the patient can receive equally good care somewhere else. Institutional treatment is preferable to taking the cure in a hotel or boarding house. With proper treatment the outcome in any particular case of tuberculosis depends largely upon that very indefinite individual factor, namely, allergy or resistance. Not all patients are equally resistant to the disease or can build up sufficient resistance even under proper treatment. Unfortunately we have no method of accurately estimating the individual resistance and must depend upon the subsequent progress of the patient to learn whether or not he possesses sufficient resistance to overcome the disease. This makes prognosis uncertain.—*Climate in Relation to the Treatment of Tuberculosis, E. P. Kolb, Long Island M. J., January, 1921, xv, 1.*

Necessity of Foundation of Sanatoria for Surgical Tuberculosis.—A year ago a questionnaire was circulated among the chiefs of the surgical departments of the canton, district, and children's hospitals of Switzerland. Fifty answers were received which are analyzed in this article. The first question, whether the care of surgical tuberculosis cases within the domain of the questioned was adequate, received 10 affirmative, 34 negative and 6 indefinite answers. The same impression is gained when the results of the statistics of Basle for 1913 are considered. Of 15,000 surgically tuberculous in Switzerland, a third are poor or of very moderate means and need mountain cure, whereas there are available at most only 500 places. Out of 100 cases with surgical tuberculosis, 3 were well-to-do, 28 belonged to the middle class and 69 were poor. As to the second question, in which direction these cases need be aided most, the necessity for sanatoria in high altitudes was emphasized by 44. At the present time there is no known means which improves the general condition and which makes possible so good functional results as sun treatment and high altitudes. The third question, whether and to what extent the existing sanatoria can be considered in the treatment for surgical tuberculosis, was emphatically denied by 40: only 4 were satisfied; the rest were indefinite. The question by whom the public sanatoria (*Volksheilstätten*) are to be founded, is in the main answered by the state organization of Switzerland: 25 recommended cantonal institutions, 15 recommended the combination of several cantons and 10 answered indefinitely. The last question, whether a Swiss combination of efforts in favor of the surgically tuberculous without means is desirable, was affirmed by 34 and denied by 6. The institution of several colonies would benefit all canons. Quervain recommends that a commission for the combating of surgical tuberculosis be nominated.—*Die Notwendigkeit der Gründung besonderer Heilstätten fur chirurgische Tuberkulöse in der Schweiz, de Quervain, Gegen die Tuberkulose, February 12, 1921.*

Treatment of Tuberculosis of the Kidney.—Winiwarter reports four cases of tuberculosis of the kidney in which catheterization of the ureters, to determine which kidney was affected, was impossible. He recommends in such cases *sectio alta* under anesthesia. Before opening the bladder he injects phlorizin and indigocarmin; he then catheterizes both ureters, passing the catheters out through the urethra. The tuberculous changes in the bladder are curetted and cauterized, and then the bladder and the abdominal wound are closed. In the meantime the urine from each kidney is collected and examined for albumin, blue staining and sugar. The functional tests should be completed by the time the preparations for nephrectomy have been made, so that no time is lost. The ureter catheters are then drawn out, a retention catheter is inserted in the bladder, and the tuberculous kidney is removed. *Beitrag zur Behandlung der Nierentuberkulose, J. Winiwarter, Wien Klin. Wchnschr., November 25, 1920, xxxiii, 1043.*

Treatment of Tuberculosis of the Bones and Joints.—Sorrel formularized his treatment of tuberculosis of the bones and joints as follows: "Immobilize in the young, resect in the adult, amputate in the aged." Lenormant does not like exacting formulas in medicine, which impress themselves on the memory but which are uncompromising in their rigidity. Sorrel's attempt to codify the treatment of tuberculosis of the bones and joints appears to him to be entirely too drastic and schematic, and, if applied to the letter instead of the spirit of the dictum, will result in absurd consequences. Why reserve for the infant and absolutely refuse to the adult the benefits of immobilization? It may be correct to resect in the adult but only when it is specifically indicated. A general rule for amputation in the aged is too drastic.—*A propos du traitement des tuberculoses ostéo-articulaires, Lenormant, Presse méd., March 19, 1921, xxix,* 221.

Blood Transfusion in Pulmonary Tuberculosis.—The transfusion of blood has been resorted to by the authors in a series of cases at the Chicago Municipal Tuberculosis Sanatorium. The blood of the donor and recipient are tested for isoagglutinins and isohemolysin, Wassermann tests for syphilis, and complement fixation tests for tuberculosis. In addition the cytology of the blood of the recipient is studied weekly. The transfusion is done by the indirect method at weekly intervals. The recipients are patients in whom the prognosis is doubtful or bad, who are not improving under the usual method of treatment and are classified as moderately advanced B and C, and far advanced A and B, according to the classification of the National Tuberculosis Association. Six patients have received from 2 to 5 transfusions at weekly intervals of from 100 to 375 cc. of blood. Transfusion of over 200 cc. usually resulted in a reaction characterized by chill, fever and sweating with prompt recovery therefrom. The clinical course in this series of cases was not appreciably altered. Changes in the blood of the recipients in this series were a steady deviation to the left or no change as determined by Arneth count. In conclusion, it is evident that normal blood is devoid of that specific element which will arrest the progress of the disease. Further experimental work is now being carried on with a series of cases in which the donors show a positive complement fixation test for tuberculosis.—*Blood Transfusion in Treatment of Pulmonary Tuberculosis, E. B. Freilich, A. J. Hruby, and J. J. Mendelsohn, Illinois M. J., January, 1921, xxxix, 32.*

What the Nurse Should Know about Tuberculosis.—The nurse should be familiar with the following facts about tuberculosis: the cause and transmission of the disease, the most common early symptoms, the broad principles of treatment, and the principles of hygiene and sanitation in general. Sooner or later her work will bring her into close contact with other social problems such as housing, city cleaning, factory conditions, cost of living, milk supply and lawmaking. She should know that the consumptive is a menace to the community and that his care is as much a public duty as that of a smallpox patient. She must realize how important it is to watch contacts and that child contacts are most susceptible and form the consumptive army of later years. Above all, she should not regard her patient as a pauper case.—*What the Nurse Should Know about Tuberculosis, E. A. Gray, Pub. Health Nurse, July, 1920.*

Knights of Columbus in Tuberculosis Campaign.—A Knights of Columbus National Committee is announced with Dr. Edward W. Buckley, St. Paul, "supreme physician" at the head, for the investigation of the causes and care of tuberculosis in the United States. This committee will act in conjunction with the national and state health services and the Red Cross.—*Medical News, J. Am. M. Ass., May 28, 1921, lxxvi,* 1507.

Trauma and Tuberculosis.—Korteweg is making an official investigation of this subject and appeals to the profession to aid him in this task. Acute miliary tuberculosis, especially in the form of meningitis, is the most instructive for this purpose, and he charts the cases he has compiled in which death occurred within six weeks of the trauma. In 30 cases of tuberculous meningitis, the trauma had been an operation; in all but 3, for a tuberculous process. In 19 cases there had been a fall or blow on the head; in 5 a fall not affecting the head; a violent shock in 3, and in one case only extreme fright for half an hour. His chart shows that the trauma cannot be incriminated for a death from tuberculous meningitis or miliary tuberculosis occurring in less than fourteen days afterward. In the 14 cases of miliary tuberculosis, the trauma had been an operation in 4; fall into water in 1 case; fall from a height in 5, and abortion in 4. The connection between trauma and acute tuberculosis has long rendered surgeons extra wary in operating on the tuberculous. The chart emphasizes further that this connection is manifested also in the duration of the disease, the fifteenth day showing the beginning of the fatalities, and the number runs up high. At the twenty-seventh day it drops abruptly.—*Tijdsverband tusschen trauma en tuberculose, R. Korteweg, Nederl. Tijdschr. v. Geneesk. January 8, 1921, lxv, 164.*

Auto-urine Test for Active Tuberculosis.—The biologic tuberculin reactions heretofore in use indicate little or nothing of the stage of the disease, of its development, of the retrogression of the process or of its healing—in other words, of the activity of the disease. The propounders of the auto-urine test theory believe it possible to demonstrate the activity of a tuberculous process through the proof of antigens in the human urine by means of an allergy reaction of the skin. This theory is the product of the idea that when there is an active tuberculous process in the body there must be products of elimination and disintegration of and due to the tubercle bacilli. These products of active disintegration or antigens, or tuberculin-antituberculins, as they are described by some, are thrown into and distributed by the blood stream, where part of them are held and made harmless by the defensive mechanism of the body, the antibodies; and part are removed from the body by the secretory organs, the kidneys, the intestines, the liver, the skin, the lacteals, etc. It follows that if the existence of these antigens can be proved, then will the activity of the tuberculous process be evident; for, unless there is an active and disintegrating infective focus in the body, the formation and elimination of antigens is not comprehensible or conceivable. The method by which the existence of these antigens is demonstrated and proved is the auto-urine reaction, depending, however, on allergy or organic hypersusceptibility of the skin. The demonstration of the presence or absence of antigens is accomplished by injecting into the skin of the patient his own urine, which has undergone certain modifications. Should the skin be anergic, then his urine is injected into another known to have skin allergy, or organic hypersusceptibility to tuberculins. Briefly, the tuberculin used for the skin reaction is furnished by the patient himself in his own urine. If this reaction is positive, the assumption is that tuberculous antigens are in the urine, and that therefore an active tuberculous process exists in the body. If the urine contains no antigens, its injection affects the skin nonspecifically and exclusively, as would an injection of a solution of various urinary salts which, if not too highly concentrated, will not cause a reaction of itself. The principles of these several theories and their development as facts are supported by findings in about 300 cases reported by Wildbolz, Lans and Imhof. The results obtained by the authors in forty cases with the auto-urine reaction are tabulated. It was observed that all cases with bone involvement were allergic, and all reacted distinctly to the auto-urine test. In none of the cases were there conflicting results. In every case in which there was definite allergy to tuberculin along with signs of activity, the auto-urine reaction was positive. And all of the anergic patients with positive signs gave definite reactions when their urine was injected into allergic individuals except in one case in which the renal impairment induced the authors to use the auto-serum test, the result of which was positive. Further, the negative reactions obtained in the allergic cases have only borne out the opinion that these individuals had no active tuberculosis and were accepted as favorable rather than as disparaging results.—*The Auto-Urine Test for Active Tuberculosis, C. B. Gibson and W. E. Carroll, J. Am. M. Ass., May 21. 1921, lxxvi, 1381.*

Infection in Tuberculosis.—This is a paper addressed to nurses. It must be gratefully recorded that tuberculosis has been at last recognized by the best schools of nursing, and some theoretical instruction made available. So now a nurse need no longer circulate in the community her traditional grandmother beliefs about tuberculosis, stamped with the authority of a uniform and a diploma. A bit of misinformation hard to correct, even among nurses, is that tuberculosis takes a place with scarlet fever, diphtheria and influenza; or perhaps even with smallpox, Asiatic cholera, and the plague as a disease easily communicable and dangerous. Tuberculosis is so infectious and so widespread that, however carefully children are brought up, few in ordinary communities reach adult life uninfected. This childhood infection, almost universal, gives a latent focus of disease which may at any age be stirred into activity by adverse conditions, but gives also, to some extent at any rate, a protective vaccination against further infection. Gross tuberculous infection in infancy is usually fatal, and the death rate up to eighteen months of age is heavier than in any other age period of equal length. It is considered that some degree of vaccination against human tuberculosis is acquired by the use of milk from cattle suffering from the bovine form of the disease. There may perhaps be seen in this some silver lining to an otherwise dark cloud. Average people, like most of us, or all of us, have quite likely a partial immunity to measles and tuberculosis infection, because we have been already infected in childhood. Reinfection may occur, but usually there is little danger except when infection is gross or resistance unusually low. So much for tuberculosis as an infection. Tuberculosis, the disease, is something quite different. From this adults are certainly not exempt. In most countries tuberculosis accounts for at least one death in four between the ages of twenty and forty. This open disease of adult years is flower and fruit of the seed planted in childhood. What then causes tuberculosis at these ages? There has been no new infection. The disease has come from within, not from without. In human soils, tuberculosis is widely seeded and rooted. Good human husbandry keeps disease under control, bad human husbandry, anything that debilitates, exhausts, breaks down, lowers resistance, makes for disease activity. If there were danger in nursing tuberculosis cases, that danger would be greater in the general hospital where tuberculosis is not expected, than in the sanatorium, where it is counted upon and every detail arranged appropriately. The freedom of sanatorium staffs from the disease is remarkable.—*Infection in Tuberculosis, D. A. Stewart, Nurses' Alumnae J., Winnipeg Gen. Hosp., 1920.*

Spontaneous Pneumothorax Complicating Artificial Pneumothorax.—Burnand of Leysin describes several cases which show the irreparable nature of an extensive opening between the pleura and lung. In 4 of his 9 cases the spontaneous pneumothorax had existed before and had developed anew in the course of the therapeutic pneumothorax. Expectoration of pus and the anomalous behavior of the manometer warned of this complication. Three of the 9 patients succumbed to the effects in the first month and 4 in from three to six months. Forlanini's 8 patients all died. The only recourse, if the pus keeps forming, is to open the pleura and drain, but this is only palliative. A favorable evolution is extremely rare.—*La perforation du poumon, complication du pneumothorax artificiel, M. R. Burnand, Ann. d. Méd., January, 1921, ix, 22.*

Immune Reactions with Artificial Pneumothorax.—Carpi found the opsonic index constantly increased in cases of pulmonary tuberculosis under treatment with artificial pneumothorax. As evidence of the immune reactions may be counted the cure of laryngeal tuberculosis during the artificial pneumothorax treatment. Even more significant is the cure of renal tuberculosis under these conditions. In one case the cure of a classic tuberculosis of the kidney was confirmed three years later. Such cases establish the stimulating action on the defensive forces and specific stimulation of the morbid foci under the influence of the changes brought about by the artificial pneumothorax.—*Réactions immunitaires dans la tuberculose pulmonaire traitée par le pneumothorax artificiel, U. Carpi, Schweiz. med. Wchnschr., March 31, 1921, li, 299.*

Roentgen Ray and Tuberculosis in Infants and Children.—As a result of a statistical study of forty-four infants and children at the Boston Consumptives' Hospital, the following points are emphasized: (1) (*a*) The Pirquet and intracutaneous skin reactions are reliable guides to infection with tubercle bacilli, and the number of positive reactions increase from infancy up through childhood, over ten years of age, all patients reacting. (*b*) In 26 of 36 positive skin reactions, the roentgen ray disclosed the site of infection to be intrathoracic. (2) D'Espine's sign as a clinical index of tuberculosis of the bronchial lymph nodes is of relatively little value, being elicited only eleven times, as against roentgen ray evidence of glandular enlargement in twenty-eight cases. (3) Three cases of positive sputum were found in fourteen diagnoses of chronic pulmonary tuberculosis. (4) Fourteen cases of chronic pulmonary tuberculosis of the adult type were found. This suggests that the so called phthisis is more common in children than has been stated by writers of textbooks. (5) Fifteen cases, negative clinically, showed definite roentgen ray signs of marked structural changes consistent with tuberculous infection. This raises the question as to whether these children are to be regarded as more likely to develop clinical tuberculosis and should thus be watched carefully and roentgenographed at fairly frequent intervals.—*Roentgen Ray and Tuberculosis in Infants and Children. A Study of Forty-Four Cases, F. W. O'Brien and F. B. Ames, J. Am. M. Ass., May 28, 1921, lxxvi, 1474.*

Tuberculosis in Children.—The author uses the following routine examination for new patients at the Children's Tuberculosis Clinic of the Michael Reese Dispensary, Chicago: Family history, previous history, weight and height, physical examination, Pirquet test, X-ray of chest. In old patients he determines the weight at every visit, the height once in three months, and makes a physical examination. The following is the routine treatment of latent tuberculosis: patients are referred to Nutrition Clinic; general instructions are given as to food and sleeping; reëxaminations are made every three months unless otherwise specified; home conditions are investigated; all other members of the family are examined. All contact cases with negative Pirquet reaction should be retained at the clinic and examined once in three months. All cases with negative Pirquet reaction with no history of tuberculosis in the family should be referred back to the Pediatrics Department. *Summary.* (1) In a study of 300 children most of whom came in contact with tuberculous people, 141 cases reacted positively to the Pirquet test and 83 negatively; 76 cases are still pending a diangosis. (2) Of the 141 cases that reacted positively, in ninety per cent the infection was only latent. Of the 14 cases of active tuberculosis, only 3 or approximately 3 per cent of the total, had active pulmonary tuberculosis. (3) In most positive cases, the source of infection was the father, although the mother was infected in a good number of cases. (4) Ninety-eight per cent of the cases with latent tuberculosis showed no subjective symptoms. (5) Ninety per cent of the cases were under weight, most of them averaging from 4 to 8 per cent below the standard. (6) Long eyelashes and visible veins over the chest were present in the greatest number of children with latent tuberculosis. (7) Seventy-five per cent of the positive cases showed hilum dulness and whispered bronchophony to the seventh dorsal vertebra. These two signs are strongly indicative of bronchial gland tuberculosis. (8) The X-ray plates usually confirmed the hilum dulness by showing a shadow over the hilum and often also one or more calcified spots in the substance of the lungs and radiations toward the apex. Although one is not justified in making a diagnosis of tuberculous glands from the X-ray examination alone, the latter should constitute corroborative evidence of the presence of tuberculous glands. (9) The Eustace-Smith sign was very infrequent in the cases of latent tuberculosis in this series. (10) Tuberculin tests when positive should establish a diagnosis of the presence of the tuberculous infection in children. The classification of the type of infection must be made by the subjective and objective symptoms and by the X-ray findings. (11) Latent tuberculosis requires no active treatment. The patient, however, should be given the benefit of general hygienic measures. (12) All children who have come in contact with a tuberculous individual should be under observation so as to establish the diagnosis and institute treatment if necessary. If the home conditions are good, children with latent tuberculosis should be left at home. If the home conditions are poor or if there is an open case of tuberculosis in the family, the children should be sent to a sanatorium.—*A Clinical Study of Tuberculosis in Children. A. Levinson, Med. Rec., May 7, 1921, xcix, 773.*

Localized Pleural Irritation and Syncopal Accidents.—Although some surgeons seduced by the simplicity of technique and the generally remarkable tolerance of the pleura to operative manoeuvres, have perhaps lost sight of the existence of pleural reflexes, others on the contrary have exaggerated the danger. Montaz and Pierry have each recently reported deaths from syncope following an injury to the pleural cavity. Montaz's patient had been hit with a bit of exploding shell and an operation of small importance for its removal, on account of rather alarming symptoms, resulted in the death of the patient a few hours later from syncopal accidents. In Pierry's case death suddenly occurred while the patient was being radiographed for a bullet in the thorax. Pierry says that the reflex, caused by splinters of bone irritating the pleura during forced breathing for the radiograph, was the cause of death, since autopsy revealed no other cause. The susceptibility of the pleura to certain local irritations, in appearance of minimum importance,—exploratory puncture, for example—has been recognized for a long time; and the accidents to which they may give rise have been minutely described by Bouveret, Cestan, Roch and others. The clinical modalities have been studied, although they have been subdivided perhaps a little artificially, but an attempt has been made to grasp the etiology and pathogenesis in order to fix upon a rational treatment. Hypotheses are not wanting for explaining these reactions, and although some are ingenious their very number sufficiently shows the complexity of the phenomena and the difficulties encountered when their internal mechanism is to be explained. There are the toxic theory, and the theories of sudden depression, embolus, and cerebral anemia, the uremic and the reflex theories, to mention the more important. In certain remarkable experiments Cordier has shown the capital part played by reflexes in the production of these accidents, the starting point of which is the irritation of the pleural terminal filaments of the pneumogastric nerves. It would seem to be a fact that this nerve is alone concerned and not the phrenic, intercostals, or sympathetic, as many have supposed. Syncopal or convulsive phenomena, hemiplegia or paretic accidents, vasomotor disturbances, minor and major nervous accidents, observed both clinically and experimentally in lesions of the pleura, are all phenomena of the same order. They are reflexes arising in the rich nerve arborizations described by Rubashkin and Romanoff, in the deep stratum of the visceral pleura, the pneumogastric being the centripetal route. Cordier very rightly insists on the essential part played by localized irritations of this serosa. Every pleural irritation is not the origin of a violent reflex; on the contrary, experience during the war has confirmed what was already known, namely, that the healthy pleura easily supports massive excitation affecting large areas, quite in contrast to the peritoneum. The study of the blood pressure during thoracotomies is a demonstration of this. While the pressure curve during laparotomies offers variations from a few centimetres of Hg. to complete symcope, according to the manipulations made on the peritoneum—traction on the intestine, mesentery, etc.—the sphygmomanometer appears to remain quite indifferent to surgical manipulations on the lungs and pleura. It, however, must not be forgotten that this is generally the case and that massive irritation of the pleura is not without its risks, even when the interference does not require the infliction of traumatic insults to the parts. Pleural reflexes explain certain serious accidents, paradoxical in appearance, occurring during thoracotomy or shortly after the thorax has been closed. There therefore exist in the pleura certain particularly sensitive areas whose excitation is susceptible of causing phenomena of shock. Their topography is not as yet clearly defined and all that can be said at present is that they exist.—*Editorial, Med. Rec., April 23, 1921, xcix, 703.*

Gastric Ulcer in the Tuberculous.—The authors have found signs of pulmonary tuberculosis in a surprisingly large proportion of their gastric ulcer cases, and they urge giving the tuberculous the benefit of operative treatment the same as if they were not tuberculous. Four cases are reported.—*Du traitement chirurgical de l'ulcus simplex chez les tuberculeux, G. Aigrot and R. Gaillard, Lyon Méd., March 25, 1921,* cxxx, *245.*

Tuberculous Peritonitis.—Cases of tuberculous peritonitis are very favorable for cure, at least if the abdominal condition is the main factor. The possibility of cure is due to the confinement of the morbid process in a place where it can be attacked by nature's forces. In areas that can be spared without destruction to life, surgical elimination is of great benefit. Thus nature can cure tuberculous peritonitis in pure form. Mixed infection destroys tissue, but added toxins are destructive to life as well as to tissue and are more chronic and difficult to treat or control. If ascites in tuberculous peritonitis adds so enormously to the surface area involved in a tuberculous process and must be overcome by changes in the peritoneum by changing the exudate from serous to fibrinous and plastic adhesion before cure occurs, such surgical treatment as will hasten the process is advisable. The important question is with regard to the permanency of cure and restoration to health. Death or even ill health rarely comes from obstruction due to the adhesions. When acute obstruction develops it is due to a single band or the hyperplastic variety without ascites. By removing the focus of disease in tuberculous peritonitis, especially when such a focus involves a tuberculous mucous membrane, a high percentage of permanency of cure with a very low primary operative mortality is secured.—*Tuberculous Peritonitis, C. H. Mayo, Minnesota Med., April, 1921, iv, 259.*

Dyspepsia from Pott's Disease.—A woman of forty-two suffered for two years from dyspeptic trouble. She had diminished appetite, fulness and pressure immediately after meals; after twenty-five minutes a sore feeling followed by cramps which radiated to the region of fifth to seventh dorsal spines; eructations, and after three to four hours epigastric burning which lasted a few minutes. Then she was fairly comfortable until the next meal, with only a vague feeling of dragging and emptiness of the stomach followed by general lassitude. As dietetic and medicinal measures had proved ineffective, she entered the hospital. There a tuberculous spondylitis of the fifth to seventh dorsal vertebrae was found with marked local pain and tenderness, without deformity, but with stiffness of spine and a positive X-ray picture. After a plaster corset had been applied, the dyspeptic symptoms disappeared as if by magic, together with the dorsal pains. The authors apply the term gastroradiculitis to this splanchnic irritation from Pott's disease.—*Gastro-radiculite d'origine pottique, F. Ramond and C. Jacquelin, Progr. Méd., April 9, 1921, no. 15, 155.*

Diagnostic Value of Tuberculin in Surgical Tuberculosis.—Ninety-nine patients were tested first with the Pirquet test and, if positive, with 1, 5 and 10 mgm. of O. T. subcutaneously. *Conclusions:* 1. A positive focal reaction is obtainable in only two-thirds of cases of surgical tuberculosis. Closed cases react more frequently than those with fistulae or abscesses. Occasionally a certain case of tuberculosis reacts focally but not constitutionally. Healed cases do no longer give a focal reaction. 2. A focal reaction which is only subjective must be accepted with great caution. 3.

If all tuberculin tests are negative, tuberculosis can be excluded with certainty; if temperature and focal reactions are absent, but the puncture reaction is positive, tuberculosis can be excluded with great probability, or healing can be assumed to have taken place. 4. An absent focal but positive temperature reaction does not speak against tuberculosis. In these cases the onset and cause of the temperature may have a limited diagnostic value. 5. The tuberculin test, carried out systematically and cautiously, is a valuable and harmless diagnostic help.—*Die Tuberkulindiagnostik in der chirurgischen Tuberkulose, C. Mau, Deutsch. Ztschr. f. Chir., March, 1921, clxi, 145.*

Tuberculous Meningitis in Adult Consumptives.—Tuberculous meningitis is discussed, as it occurs (1) in children and (2) in adults, (a) with more or less extensive pulmonary tuberculosis or (b) with previously good health. This makes possible the isolation of the factors which a concomitant pulmonary tuberculosis adds to the symptomatology and course of the disease. Between 1910 and 1919, 30 cases of tuberculous meningitis were observed in persons over the age of sixteen. Fourteen cases are analyzed in which the diagnosis was confirmed by autopsy. Twelve of these patients were in the third stage, and the remaining two in the second stage of pulmonary tuberculosis. Three typical cases are reported. Delirium was characterized by its quietness. The changes in the pulse rate were not constant and may have been obscured by the preexisting pulmonary disease. In some cases, retention of urine and feces occurred. The two cardinal symptoms, cervical rigidity and Kernig's sign, were not invariably present. In several cases rigidity of the neck was present one day and completely absent the next. Headache was the most constant symptom, but in several cases it was intermittent. Vomiting was common. The symptom which dominates the clinical picture after the disease is well developed is drowsiness. Tuberculous meningitis in adult consumptives cannot be regarded as latent. There is a definite difference in the clinical picture of tuberculous meningitis in children and in adult consumptives. The extent and distribution of the disease appear to have little effect in determining the severity of the symptoms. In some cases the terminal stage of toxemia in pulmonary tuberculosis may evoke a clinical picture indistinguishable from that of tuberculous meningitis without the aid of lumbar puncture.—*The Symptoms and Course of Tuberculous Meningitis in Adult Consumptives, C. Holten, Tubercle, January, 1921, ii, 150.*

Psychogenic Pseudotuberculosis.—Several years ago a young woman of unusually sound health received the news that a relative had dropped dead. She bore the experience with fortitude and was soon back at her occupation. However she rapidly developed a syndrome of acute phthisis with progressive emaciation, cough, and night sweats, so that her physician on her first visit to him was almost convinced that she was tuberculous. He deferred giving his opinion until the next visit, when he found the patient quite free from symptoms, and the psychogenic nature of the latter became apparent when the patient later presented another syndrome of cardiac stasis, which passed off and left her in her usual health. During the latter experience she had gone about her daily business with ankles so swollen that she could not button her shoes. Both syndromes cleared up spontaneously.

In the November 13 number of the *Bulletin Médical* (xxxiv, 53) de Fleury has a paper on false tuberculosis of psychopathic nature and a comparison of his findings with the above mentioned case should be of interest. This author sketches his type as follows: At the tuberculous age a young man or woman begins to decline in health which, let us say, has never been robust. There is a condition of lassitude, fatigability, and anemia which disquiets the relatives. The patient seems to slip into the state of tuberculosis. But this type is not the one which really interests the author. There are young people whose health is vigorous and whose high spirits make them conspicuous, who shock their friends by passing without warning into a state of malnutrition. In such cases the author expressly states that no psychic shock or vexation has preceded the symptoms, no physical overstrain, nothing to accuse in connection with the sudden failure of health. Relatives and friends become alarmed and summon medical counsel. Examination proves negative. The condition progresses and in some respects suggests Graves's disease, presenting symptoms common to both it and incipient tuberculosis, such as tachycardia, sweating, etc. Tremor may be marked. The patient is impressionable and becomes badly frightened over his condition. The symptoms are conflicting enough. Fever may be absent. Low blood pressure is usually found. To give the patient the benefit of the doubt he is given sanatorium treatment under which he does not prosper. He cannot be made to gain a pound and his neurotic symptoms seem out of proportion to the disturbances of general health. One might term the patient a tuberculo-neurasthenic with his peculiar mental state, insomnia, tremor, etc. A consultation held between an expert phthisiologist and neurologist will bring out the fact that the condition is purely neurotic. The cough is a nervous cough and the subject can be diverted so that it will disappear. Tachycardia, night sweats, anorexia are all psychogenic. The condition of hypochondria is the very reverse of the optimism of the tuberculous. The author especially states, however, in connection with the mental depression, that it may be cyclothymic and be followed by a wave of mental exaltation. During this phase the tuberculous syndrome recedes. Under the circumstances one might wrongly conclude that the patient's optimism was the direct result of recovery. It is evident that these endogenous cases of de Fleury have hardly anything in common with the case cited by the editor in which a very shortlived imitation of beginning tuberculosis occurred in a nonneurotic subject as the result of psychic trauma.—*Editorial, Med. Rec., January 29, 1921, xcix, 189.*

Involvement of Genitourinary Tract in Active Pulmonary Tuberculosis.—During eleven months of Peterson's service at Fort Bayard, the patient population varied between 800 and 2000, practically all in the original draft age (from twenty to thirty years). Approximately 80 per cent of the patients had active pulmonary tuberculosis; the remainder were sent there for observation. Peterson demonstrated only five cases of surgical tuberculosis of the kidney, in only three of which was there active lung involvement. One man had bilateral renal tuberculosis and one had a unilateral renal tuberculosis and tuberculous epididymitis, with no active pulmonary lesions. Involvement of the epididymis was observed in three cases. On one man an epididymectomy had been performed elsewhere and a fistula persisted. One man had bilateral involvement, and in one an acute abscess developed, destroying both the epididymis and testicle. A castration was done and the wound healed in three weeks. Two months later the patient died from an acute tuberculous pneumonia. At necropsy the kidneys were free from tuberculous invasion. The prostate showed a caseated abscess and there was a cold abscess at the stump of the cord following the castration, which had not pointed to the surface. At necropsies massive lung lesions were always found—old multiple cavities filled with pus, cheesy material and necrotic tissue and large walled-off cavities with very extensive destruction of tissue. These old types of lesions were now and then associated with a fresh general miliary distribution, both into the remaining functioning lung tissue and into the peritoneum and abdominal viscera. Except in cases where acute miliary tuberculosis was the immediate cause of death, the genito-urinary tract was rarely involved in the infection, and here the lungs showed old massive lesions, while the lesions in the kidneys were of the young or miliary type.—*Involvement of Genito-Urinary Tract Associated with Active Pulmonary Tuberculosis, A. Peterson, Cal. State J. of Med., January, 1921, xix, 18.*

Vaginal Tuberculosis.—The disposition to genital tuberculosis is greater in the female than in the male; in most cases the lungs are coincidently involved. It occurs in the following order of frequency,—the peritoneum, intestines, and last the genital organs. The highest incidence is during the ages of twenty to thirty years. Any part of the genital tract may be involved separately or combined. The tube is the most frequent site of involvement, then the ovaries, cervix and last of all the vagina.—*Über Vaginaltuberkulose bei weiblicher Genitaltuberkulose, T. Poetz, (Inaug. Diss., Bonn, 1919), Zentrabl. f. Chir., 1920, xlvii, 359.*

Genesis of Tubal Tuberculosis.—Tuberculosis of the Fallopian tubes is a secondary disease. It results as a rule from an influx of bacilli from the peritoneum, or by continuity from the uterus, or from distant foci by way of the blood or the lymphatics. Tuberculous peritonitis is the most common source of tubal tuberculosis and usually leads to an infection of the tubal mucous membrane, whereas hematogenous infection involves the deeper tissues primarily. Of 222 postmortems on women, 50 with florid tuberculosis, the tubes were involved in 15 or 30 per cent which is a much higher percentage than that reported previously in the literature. The incidence of tubal tuberculosis was greatest in the thirty to forty year period of life. Fifteen cases are tabulated. The ages of most of the patients varied from thirty to sixty; one each was respectively five, six, seventeen, twenty-six and seventy years old. Tubal tuberculosis was found associated with pulmonary tuberculosis in 15 cases (100 per cent), with intestinal tuberculosis in 14 (93 per cent), with tuberculous peritonitis in 12 (80 per cent), with genitourinary tuberculosis in 1 (65 per cent), with generalized miliary tuberculosis in 4 cases (27 per cent).—*Ein Beitrag zur Frage über die Genese der Tubentuberkulose, V. Kafka, Arch. f. Gynäk., 1920, cxiii, 490.*

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The Abstract Editor is Dr. George Mannheimer, 41 West 51st Street, New York City. Prompt transmission to him of reprints or abstracts of papers on tuberculosis, sanatorium or board of health reports, etc., will promote their early publication in this section.

Abstracts should be sent typewritten on one side of the page only. They should be as concise and compact as the subject matter of the article warrants. They should be headed with a short title, and followed by the full title of the paper, author's name, journal, date, column and page

Case of Urological Tuberculosis.—A woman of twenty-nine was found to be suffering from tuberculosis of the left kidney and bladder in October, 1916. The symptoms had then existed for six months. The left kidney was removed January, 1917. The patient gained 30 pounds and lost many of her painful symptoms. In May, 1919, the symptoms returned. In October, 1919, the right kidney was found enlarged and the right ureteral orifice ulcerated. Instillations of 5 per cent phenol solution were given into the bladder with marked improvement at first, but had to be discontinued later, on account of the pain they produced. At the end of three and a half years the patient was as badly off as at the beginning of symptoms. The case shows the unsatisfactory state of treatment of bladder and kidney tuberculosis.—*Report of a Case of Urological Tuberculosis, M. Zigler, Med. Rec., May 14, 1921*, xcix, 835.

Renal Tuberculosis.—*Conclusions*: (1) Renal tuberculosis is very common and especially so during the third and fourth decades of life. There is practically no difference in the relative incidence of nontuberculous pyonephrosis, renal lithiasis and renal tuberculosis. Lesions pathologically classified under these three heads constitute about 70 per cent of all surgical lesions of the kidney. (2) Vesical rather than renal symptoms predominate. If both vesical and renal symptoms are present, the vesical symptoms will antedate the renal symptoms in the majority of cases. Occasionally there are no symptoms from either the kidney or the bladder, the patient merely complaining of loss of strength and weight. (3) Fewer mistaken diagnoses will be made and the duration of the disease before diagnosis will be shortened if cystoscopy is performed in every case where the pathological urinary findings remain unchanged or only slightly so after several treatments of the bladder. (4) If the catheterized bladder specimen shows pus and no bacteria, and is negative on culture, cystoscopy should be performed without treating the bladder, unless the cystitis demands palliative treatment preparatory to cystoscopy. If the bladder urine shows tubercle bacilli, of course ureteral catheterization and functional tests should be performed as soon as possible. (5) Since typical shadows occur in about 20 per cent of cases of renal tuberculosis, radiograms should be made before cystoscopic examination whenever possible. (6) Even though 70 to 80 per cent of these patients have constitutional symptoms such as loss of weight and strength, fever, chills, and night sweats, it is unfair to the remaining 20 to 30 per cent who are in fair or excellent health to await such constitutional symptoms before making a diagnosis. (7)

Repeated microscopic examinations of the urine, following the method of Crabtree, will show the tubercle bacillus in 75 per cent of cases. (8) Naturally, guinea pig inoculation will be negative unless the tubercle bacillus is present and if present it will probably be found under the microscope if diligently searched for, provided a good technique is used. Consequently the guinea pig test is not often indicated, since it is a slow and somewhat uncertain method.—*The Signs and Symptoms of Renal Tuberculosis: a Review of 125 Reported Cases, W. T. Briggs, Kentucky M. J., April, 1921, xix, 200.*

The Symptoms of Tuberculous Meningitis in Adults.—The classical symptomatology of tuberculous meningitis met with in children is occasionally realized in adults, but this is rare. It must be admitted that when it does occur it is obscure, while in advanced phisthis it is often overlooked. The majority of cases in adults give rise to purely motor accidents. such as hemiplegia, with or without Jacksonian epilepsy and radial paralysis. In other instances the hemiplegia may be either right or left brachial or crural monoplegia, chorea, athetosis, or finally a comatose state. Some patients begin with aphasia or verbal deafness, or the process at the outset may assume the clinical aspect of cerebrospinal meningitis. From this enumeration it is evident that the onset of tuberculous meningitis in adults it far from being like that met with in children. Perhaps, as Chantemesse has pointed out, there may be an early premonitory phase during which an attentive examination might have detected disturbances of the intellect or affectivity, but this is not common, although a few instances have been recorded by Vivant in particular. It is evident that the kind of onset will considerably influence the evolution of the process. A patient suddenly develops coma and dies in a few days without regaining consciousness, but aside from such tragic circumstances there are a number of varieties and forms, intermediary, so to speak, which have a duration of five or six months from the onset to the time of death. For example, a patient may be seized with a right hemiplegia, preceded by an attack of epilepsy, and remain without any change for five months, when coma develops and death occurs some days later. Nothing can be found in the general condition of the patient or the hemiplegia that throws any light on the true cause of the condition. In most instances the hemiplegia is of the limp variety without increase of the reflexes and with Babinski's sign present, while the frequent association of convulsive and paralytic phenomena is hardly sufficient to enlighten the clinician as to the real nature of the affection. Occasionally cases are met with where the paralytic phenomena of the onset are followed by significant symptoms, such as persistent headache, unequal pupils, vasomotor or sphincteric disturbances, stupor, etc., testifying to a tuberculous implication of the meninges. What is striking is the absence, at least at first, of meningeal phenomena. Hemiplegia, monoplegia, chorea, aphasia, etc., are the various conditions presented by the patients. The situation may improve for a while, but after a certain lapse of time the patient dies in coma, or, on the other hand, the affection becomes confirmed by the appearance of meningeal symptoms. Then the symptomatic picture becomes clear and vasomotor disturbances, typical cerebral vomiting, unequal pupils, Kernig's sign, and finally coma successively complete the clinical picture. The temperature chart has nothing characteristic. At times there is hardly any rise until toward the end of the process; at others there is a temperature oscillating around 102°, with remissions to normal; then the mercury rises to between 102° and 104°, and there remains. Occasionally a curious phenomenon occurs: the temperature, which was high, insensibly drops and death takes place in hypothermia. No indications can, therefore, be deduced from the temperature, but what is really interesting and implants a special stamp upon these cases of meningitis is their manner of onset, so that in this respect, aside from the classical form rare in adults, a series of forms may be described based principally on the kind of onset offered: The first is the *latent* form, which does not declare itself for a long time, then suddenly breaks out in an apoplectiform, epileptiform, or delirious attack, rapidly followed by fatal coma. The *delirious* form, in which for months there is no other manifestation than perversions of the intellect or affectivity, or a variable degree of delirium, often ending in acute mania. The *spinal* form, which is most commonly encountered in tuberculous subjects and presents the clinical aspects of ascending myelitis. And finally, the *hemiplegic* form characterized by the localization of a patch of meningitis over the psychomotor zones. Jaccoud describes a *slow and remittent* type in which a phthisical patient is seized with headache, vomiting, and weakness which last for several days and then remit, only to recur five to eight days later. After several similar attacks the meningeal symptoms appear. In Jaccoud's *sudden delirious* form a tuberculous subject is taken with intense headache lasting for twenty-four hours, then coma for one or two days, followed by violent delirium, and after a few hours coma and death supervene. This observer also describes a form the initial phenomenon of which is either an epileptiform or an aphasic attack, and still another that he calls *latent*, with two modalities, one with headache, aggravation of the general condition, but no fever; ths second with gastric disturbances and headache, also apyretic. The patient weakens and finally is carried off by some cerebral symptom. Such are the various clinical types of tuberculous meningitis in adults, the latent forms expecially characterizing the process in subjects at this time of life.—*Editorial, Med. Rec., May 7, 1921, xcix, 790.*

Nontuberculous Cold Abscesses.—Audain contributes an article on pseudotuberculosis of the cellular tissue to the *Gazette des Hôpitaux* for January 18–20, 1921, xciv, 6. The condition referred to appears to be relatively new. The clinical expression is cold abscess followed by fistulation. In such cases failure to find Koch's bacillus at first suggests some fungous infection, but in the cases referred to the author has never found any evidence of mycosis. The culture and inoculation methods have invariably been negative. The age of selection seems anywhere from fifteen to forty-five and the author has seen many cases among the indigenous inhabitants of North Africa. While usually small—the size of an egg or mandarin orange—the author has seen abscesses which gave exit to a quart of pus. The physical appearance of the latter recalled a fungous infection, rather than tuberculous pus. Clinically it was impossible to exclude tuberculosis, and the fistula or ulcer formed after evacuation also resembled exactly that of tubercle. The golden hue of the pus was the only feature, aside from negative microscopic finds, to cause suspicion of the nontuberculous nature of the process. The possibility of syphilis never even suggested itself seriously. The author recalled that cold abscesses have at times been traced to the staphylococcus, but this organism could not be accused in these cases. The condition responded well to the treatment of tuberculous cold abscess. The abscesses are often multiple and no very deep seated lesions have been seen, although the author believes that a case of empyema may have been of this character. It is possible, of course, that the tubercle bacillus or some undescribed fungus may have been responsible, even although all attempts to locate them repeatedly failed.—*Editorial, Med. Rec., April 9, 1921, xcix, 615.*

Pulmonary Syphilis Simulating Tuberculosis.—Three cases are reported from the Phipps Institute and the following conclusions are arrived at: (1) Syphilis of the apices of the lungs is not by any means a rare condition and there are many cases of this disease being treated for pulmonary tuberculosis. (2) We should avail ourselves more frequently of the Wassermann and other blood tests in private practice in cases giving signs and symptoms of active tuberculosis but not giving positive sputum. This should be done whether a history of a primary luetic lesion is obtainable or not, realizing that syphilis is often innocently acquired. Signs of an aortitis, of a perihepatitis, or of weak or suppressed breath sounds, should make us suspect syphilitic infection. By pursuing such a practice there is no doubt that we will arrest some cases which are running a rapidly downward course.—*Syphilis of the Lungs Simulating Tuberculosis, H. M. Minton, N. York M. J., June 1, 1921, cxiii, 813.*

Pulmonary Syphilis.—The author has been making a systematic search for lung syphilis since 1916 by including this disease as a possibility in every lung examination. Several fundamental facts soon became apparent: 1. The peculiarities in the anatomical structure of the lung, as demonstrated by Miller, with the relations between bronchi, arteries and lymphatics, have an intimate bearing on the interpretation of the shadows of all pulmonary lesions, including lung syphilis. 2. The characteristic method of invasion of active syphilis, wherever found, by extension along the arteries, is distinctly different from the extension of tuberculosis through the lymphatics. A consideration of the relations of lymphatics and arteries to the pulmonary subdivisions which are involved indicated that there would be a distinct difference in the shadows of these two diseases. 3. Aside from the pathological differences, the clinical observation had been that the lesions of tuberculosis and syphilis occurred, as a rule, in different parts of the lung, the former in the upper and the latter in the lower lobes. 4. The characteristics of the shadow of tuberculosis being already definitely established, the differentiation would be between syphilis and other less common types of lung disease. The following therapeutic suggestions were derived: First, in the treatment of systemic lues, it is important to know whether the lungs are involved, since a Herxheimer reaction in the lungs may be serious. Second, it is doubly important, in tuberculosis, to ascertain whether the patient combats this comparatively benign single infection or whether a sinister combination with active syphilis must be treated. Third, it may be triply important not to disturb the fibrotic changes of latent syphilis by arsenical treatment, if the tendency of this fibrosis is to arrest the tuberculosis.—*X-Ray Shadows of Lung Syphilis and Syphilitic Tuberculous Symbiosis in the Lungs, W. W. Watkins, Am. J. Roentgenol., May, 1921, viii, 259.*

X-Ray Treatment of Pulmonary Tuberculosis.—For seven years the author has been treating consumption with X-rays and claims decided benefit for most of them. He gives three treatments a week, alternately exposing the anterior and posterior chest, using 2 to 3 m.a., 6 inch spark, 15 inches in diameter, 5 to 10 minutes time, and 3 mm. of aluminum as filter.—*X-ray Treatment of Pulmonary Tuberculosis, W. Wilkinson, Am. J. Roentgenol., May, 1921, viii, 241.*

Induced Pneumothorax.—Lung lesions heal but slowly because the constant distention of the organ renders coaptation of the diseased parts impossible. By the induction of a successful collapse the following results are accomplished: the diseased lung is put at rest, coaptation of diseased surface is made possible, inflammatory or necrotic material is expressed from the alveoli or from cavities, absorption of toxins is inhibited, further extension of the disease is arrested and hemoptysis is prevented. Artificial pneumothorax is a valuable adjuvant in the management of selected cases of advanced pulmonary tuberculosis in which other measures have been of no avail. It frequently gives temporary symptomatic relief, but very rarely brings about a cure. In lung abscess its dangers outweigh its possible good effects.—*Induced Pneumothorax in the Treatment of Pulmonary Tuberculosis, B. Stivelman, N. York M. J., April 6, 1921, cxiii, 521.*

Tuberculosis and Decalcification.—That tuberculosis is to a certain extent a state of decalcification was shown by Ferrier. Pochon discusses the subject in the *Journal de Médicine de Paris* for March 10, 1921, xl, 7. The belief in a lack of lime in the tuberculous organism does not tally very well with the facts, according to Pochon. The recent famine conditions in Europe have been responsible for much tuberculosis and various conditions of the bones of a decalcifying character, but the two classes of patients seem quite distinct. We sometimes see the statement that scrofulo-tuberculous children often present a slight degree of rickets. To convince one that the average tuberculous individual is more decalcified than the average man it would be necessary to show the coexistence of the deformities of late rickets, brittle bones, etc. Pochon gives an account of a highly tuberculous family in which the disease must have spread from person to person. The normal growth rate and the absence of stigmata of rickets, etc., apparently went to show that the lime metabolism had originally been normal. One of the children, who was known to have been tuberculous at the age of eleven, later became robust, and at the age of nineteen was able to play football. During a game of the latter he developed a fracture which could only be understood by the presumption of fragile bones. Radiographs showed absence of callus during the healing process and the entire skeleton showed low lime content, judging by the weak shadows. The fracture failed to unite firmly, and after six weeks in plaster a second dressing of the same kind was necessary and at present the patient is wearing a brace. There is no pseudoarthrosis but union is not firm and the limb cannot be trusted to withstand a strain. At a later period tuberculosis brusquely reappeared in the lungs, as if associated with the poverty in lime of the organism.—*Editorial, Med. Rec., May 28, 1921, xcix, 925.*

Creatinin in Pulmonary Tuberculosis.—Three groups of five cases of pulmonary tuberculosis, uncomplicated as far as could be determined clinically, were selected in accordance with Rathbun's classification, as representing three progressive grades of disease activity. The cases were all males and care was taken to select no patients showing evidence of obesity, and to exclude adolescent and senile types. On the basis of the data secured in the study of these cases, it seems that, in apparently clinically uncomplicated cases of pulmonary tuberculosis, the creatinin coefficient is slightly below the average normal figure, and that it reaches its greatest height in middle-grade cases, that is, those in which increased katabolism, due to disease activity, has not yet been offset, by excessive tissue waste and generally lowered vitality.—*The Creatinin Coefficient in Pulmonary Tuberculosis, T. Raphael and Nina Eldridge, Arch. Int. Med., May 15, 1921, xxvii, 604.*

Control of Cattle Tuberculosis.—Pennsylvania began an active campaign to control tuberculosis in cattle in 1896. Since then this work has been continued as rapidly as funds, authority and assistance would permit. During the period from 1896 to

1919, 272,895 cattle were tested with tuberculin under state supervision. Of this number, 32,392 failed to pass the test. Tuberculin testing met with considerable opposition at first, but practically all of the earlier objections have proved to be unfounded. Tuberculin is not infallible. It is considered about 95 per cent accurate. Its greatest degree of accuracy will be found in animals that have not been previously tested. It is not unusual for a dangerous spreader of the disease to pass a satisfactory tuberculin test. For a number of years only subcutaneous tests were used; when retests were necessary the dose was doubled and ln some cases quadrupled; but it was not possible to increase the dose sufficiently to detect all infected animals. Later the intracutaneous and ophthalmic tests were introduced and have proved most helpful. In heavily infected herds a combination of two or all three of these tests is often used with excellent results. In general, the subcutaneous test is considered the most reliable of the three. The ophthalmic test is perhaps the least reliable for the reason that the reaction lasts but a short time. The reaction to the intracutaneous test remains three or four days. It is recognized and accepted by a number of states. Pennsylvania has not yet decided to accept it for cattle for interstate shipments and recommends its use only in combination testing. A well-marked reaction to any of the three tests is considered reliable evidence that the animal is affected with tuberculosis. The state has never attempted to force herd owners to submit animals to a tuberculin test. The best progress has been made in coöperation with the owners. The manner of handling tuberculosis is known as the Pennsylvania plan. Thirteen hundred herd owners have signed an agreement to such a plan; their herds having been tested in some cases more than once. There are 22,000 cattle in these herds, 8 per cent of which failed to pass the test. Animals that react to the test are slaughtered under state or federal supervision; the owner is entitled to all receipts from the hide, carcass and offal. It is generally understood that tuberculosis is communicable from animal to animal, and that if it is allowed to run unchecked in a herd it will eventually render a large percentage of the animals unprofitable and worthless. Any measures for controlling it must be based upon a practical application of the principles of bacteriology. The better these facts are known the better will be the results obtained in controlling the disease.—*Measures for the Control of Tuberculosis in Cattle, C. J. Marshall, N. York M. J., April 6, 1921, cxiii, 525.*

Tuberculin Hypersensitiveness.—Summary and conclusions: 1. When a guinea pig with well developed peritoneal tuberculosis is injected intraperitoneally with about 20 cc. of a heavy suspension of a virulent tubercle bacillus death occurs within twenty-four hours or the animal becomes extremely toxic. Such a peritoneal tuberculosis develops in about 1 month after 1 cc. of a very heavy suspension has been introduced into the abdominal cavity. If the viscid fluid which is contained within the peritoneal cavity is mixed with saline solution and passed through a Berkefeld filter a bacillus-free filtrate is obtained which induces in normal guinea pigs a certain degree of cutaneous hypersensitiveness to tuberculin. 2. The abdominal organs and the parietal peritoneum to which masses of leucocytes and tubercle bacilli are adherent, when crushed and extracted with saline solution, yield a filtrate which likewise induces a cutaneous hypersensitiveness. 3. The cutaneous hypersensitiveness does not appear before the seventh or eighth day after the filtrate injection and is therefore considered to be the result of an active sensitization of the animal.—*Tuberculin Hypersensitiveness in Nontuberculous Guinea Pigs Induced by Injections of Bacillus-Free Filtrates, F. A. McJunkin, J. Exper. Med., June, xxxiii, 751.*

Studies in Immune Biology, Disposition and Constitution and Tuberculosis.—Immune biology seeks to explain the interaction of two living beings. A complete explanation of this interplay will probably never be possible by it. Constitutional pathology seeks to understand the relationship between development of disease and the peculiarities of the human body. This explanation will probably also remain incomplete. The understanding of these interactions is of great importance for the control of infectious diseases. Natural and acquired immunity are basically different. The former is the absence of cells sensitive to stimuli in vital organs. The latter is increased ability to resist. The former affords absolute protection, the latter only relative protection in most infectious diseases, which can be overcome by the vigor of a new attack. The conditions in tuberculosis are most variable. Here the biologic relations frequently undergo fluctuations for years and decades without definite final decision. A body is called predisposed to an injurious external agent when it shows less resistance to these agents than the average. The conception of disposition excludes strictly the presence of that disease. Its practical application and correct limitations meet with great difficulties. This is especially true of diseases which develop slowly and may exist for considerable time without striking symptoms. The conception of disposition of organs has been similarly misunderstood. While the importance of constitution is generally admitted there is at present no uniform understanding of it. Some conceive constitution as a changeable condition of the body, resulting from the sum of all inherited and acquired characters and modes of reaction. Others understand by constitution an original unchangeable condition determined by the germ plasm of the parents. Constitution influences resistance. Are acquired properties predisposing factors or signs of existing disease? Both possibilities may occur in one and the same case. The difficulties to be overcome by studies in constitution are of a nature similar to those of immune biologic studies. In the study of tuberculosis at first the bacteriological standpoint, and later the one-sided disposition and constitution studies were overemphasized. It is a question of attack and defense. Tubercle bacilli and the human body have been reacting upon each other for thousands of years with resulting mutual adaptation. There is no absolute immune protection against tuberculosis; only a conditional one. Tuberculosis, as it affects us, is characterized by slow development, absence of symptoms for years and tens of years, and a changeable course. The chronic forms of tuberculosis may hinder the development of the growing body in various ways, and may produce a variety of earmarks of a weakened body. It is often difficult to decide whether these earmarks are sequelae of an existing tuberculosis or whether they are predisposing factors, produced on a different basis. While it is conceded that congenital predisposition to tuberculosis is possible, it must be assumed that in some cases congenital infection with tuberculosis occurs. Similar questions, difficult to answer, come up, when congenital and unalterable constitutional predisposition is considered. Is the weakened, less resistant constitution a heritage from the germ cells of the parents, or is it a result of disease of the growing body? Here again both conditions are possible and may in rare cases coexist. An example of the most frequent weak constitution is the asthenic type of Stiller-Wenckebach asthenic constitution found to be frequent in the Frieslander. No tuberculosis without asthenic constitution was observed in them, but numberless cases of asthenic constitution without tuberculosis were found. In the Alsatians asthenic constitution is rare but tuberculosis common. The constitution is unalterable. If it is considered to be of prime importance, our struggle against tuberculosis becomes hopeless. On the other hand we are able to influence sequelae of primary stages of unrecognized tuberculosis by timely prophylaxis and treatment. Prophylaxis against infectious disease consists in removing the causative organism, or in protecting the individual against the action of the organism. Neither can be accomplished perfectly in the case of tuberculosis. But we must endeavor to render innocuous the seriously ill with active sputum from whom massive and repeated infection can arise. Any measure leading to increased power of the cells and decreased power of the invading organisms offers prospects of success. The mode of life certainly influences the general capacity of the body and the ability to resist tubercle bacilli. The majority of the tuberculous who are in dire need of sanatorium treatment do not receive it, while a large number of the tuberculous are taken care of in sanatoria long after they have ceased needing such treatment. The chronic tuberculous person has the best prospects of permanent recovery under conditions of life which he is accustomed to. In immune biological treatment various forms of energy are employed. Mechanical, physical, chemical and biological remedies are allowed to act on the diseased body and especially the involved foci. In the varying sensitiveness of the tuberculous body to specific stimuli we possess a method of regulating the relationship between attack and resistance. We must distinguish between favorable and unfavorable decrease of sensitiveness—positive and negative anergy. The employment of specific stimuli is most difficult, but also most promising. Rigid rules are out of place, because the conditions in the individual cases are too varying. We possess no prophylactic or active treatment applicable in all cases and under all conditions.—*Immunbiologie; Dispositions- und Konstitutionsforschung; Tuberkulose, H. v. Hayek, Berlin, 1921; Verlag von Julius Springer.*

Rôle of Immunity in Tuberculosis.—In this paper some of the current views on the rôle of immunity in tuberculosis are presented. Immunity carries with it, as a corollary, localization. Immunity is always relative. Complete immunity to any disease does not exist. Tuberculosis localized in the lungs presupposes a certain amount of immunity. It is believed that every adult will react to tuberculin if given often enough and in sufficiently large doses. The acquisition of immunity to tuberculosis begins very early. It has been observed that in a family of healthy children who become exposed to tuberculosis by a consumptive living in the house, the children over four years were unaffected by the direct exposure while those under that age suffered an impaired development. Every child has abundant opportunity for infection. Children in healthy surroundings have a better chance of getting a small infection and better vaccination. Bushnell holds that once living tubercle bacilli gain entrance to the body, they or their progeny remain in the body in a living state and so promote and maintain immunity. If the tuberculous subject were capable of entirely eradicating his tuberculosis, he would lose his immunity and thus render himself susceptible to a new infection. It is not unusual to find tubercle bacilli circulating in the blood of individuals who have not and do not develop severe tuberculosis. It is believed that transmission of pulmonary tuberculosis to adults through transient association with that disease does not exist. The results of the antituberculosis campaign have been somewhat disappointing. Recent improvements in the social and hygienic condition of the working classes who constitute the majority of the candidates for the disease must be a factor in the future, if not in the present, tuberculous morbidity and mortality. But the adaptation of people to city life and to tubercle bacilli is perhaps of greater importance than all the factors taken together, in bringing about the mortality reduction which has occurred.—*Some Observations upon the Rôle of Immunity in Tuberculosis, H. F. R. Watts, Boston M. & S. J., March 10, 1921, clxxxiv, 241.*

Tuberculosis Immunizing Vaccine.—Since 1906 human, bovine and avian tubercle bacilli have been subcultured by the author every month. The present growths represent the 184th generation. The growths are still luxuriant and true to type, but they do not produce tubercles and are completely nonpathogenic to animals. The pathogenicity has been tested every year. No change was noted until the 94th generation. After that time attenuation became marked, and after a year or two the cultures were avirulent. Treatment of disease by vaccines prepared from attenuated organisms naturally means that the production of antibodies will take place rapidly without any preliminary shock to the system, such as invariably follows the injection of vaccines prepared from virulent strains of bacteria. With a view to elucidating the real amount of tuberculosis in man caused by the human and bovine types of bacilli, and also as to immunity produced by one infection toward the other, Raw instituted clinical observation on a large scale in a Liverpool hospital of 900 beds, of which he had charge for eighteen years. In no case of primary pulmonary tuberculosis did he observe, during the course of the illness; tuberculosis of bones, joints, glands or skin, nor any instance of meningitis. Among the surgical cases of tuberculosis, 28 developed lung symptoms and 25 died. In all cases the infection of the lung was either by direct extension from cervical lymph nodes to the apex of the lung, or from a primary focus in the abdomen extending upward through the diaphragm to the bronchial nodes and lungs. This large clinical experiment convinced Raw that the human body is attacked by two quite distinct forms of tuberculosis: the one conveyed from person to person by direct infection and attacking chiefly the lungs, and the other conveyed by milk from tuberculous cows, and developed in the first few years of life. These two diseases are caused by different types of tubercle bacilli which will not live in the body at the same time; and one disease produces immunity to the other. Hence, Raw always uses a vaccine prepared from bovine cultures in the treatment of the human infections and vice versa. The vaccine which he has had prepared from his attenuated cultures is an emulsion of the bacilli, and contains all the products of the bacillus. It is nontoxic and avirulent, and produces no reaction even in large doses. For purposes of immunization in susceptible children 6 injections are given at weekly intervals. This course is repeated in 3 months. The doses recommended are 0.001, 0.002, 0.003, 0.004, 0.005, 0.006 mgm. No symptoms have been observed to follow these injections. In the treatment of the active disease the doses are much larger than have been possible up to now. At least 12 injections should be given at intervals of seven days in doses increasing from 0.001 to a maximum of 0.025 mgm. The vaccine should be freshly prepared from the cultures and should not be used after one month. It can be used with complete safety in any stage of the disease, and even in advanced cases great relief from night sweats and toxic symptoms have been noted. The results in suitable cases are excellent. Raw has succeeded in immunizing completely highly susceptible animals by the use of attenuated cultures, and he firmly believes that if all children with a tuberculous history could be safely vaccinated in the manner described they would be placed in a better position to resist infection at home.—*A Tuberculosis Immunizing Vaccine, N. Raw, Brit. M. J April 23, 1921, no. 3147, 594.*

The Operative Treatment of Pulmonary Tuberculosis.—In judging the success of operative treatment of pulmonary tuberculosis it must be remembered that the disease has usually progressed to a considerable degree and has withstood all other attempts at treatment. Jessen discusses the following methods of operative procedure: extirpation of the tuberculous lung, opening of cavities, artificial pneumothorax, extrapleural thoracoplasty, filling of cavities and pleurolysis, extrapleural pneumothorax with thoracic fistula, phrenicotomy, stretching of the sympathetic nerve and operation on the intercostal nerves, ligation of the pulmonary artery and similar methods, and widening the upper chest aperture. Extirpation of a large portion of the lung necessitates simultaneous thoracoplasty which makes the procedure a major one. If it is not possible to remove the tuberculous focus radically the next task is to avoid further absorption of toxic products. The chances for opening tuberculous cavities in general are poor, except in the case of isolated cavities, bound by adhesions. Therapeutic pneumothorax is a much safer and more promising method. It is the surgical procedure in pulmonary tuberculosis which must be considered in every case before deciding on any other method. Probably no case should be under pneumothorax pressure less than eighteen months, although the author has seen connective tissue changes after four months. The most important property of artificial pneumothorax is its detoxicating effect; therefore, compression of the outgoing blood and lymph vessels rather than simple collapse of the lung must be aimed at. The most important obstacle to the success of pneumothorax is adhesions of the pleura. In some patients with adhesions a multiple pneumothorax with many chambers can be produced. Sometimes adhesions can be removed surgically, but in general the author warns against bloody intrathoracic removal of adhesions. The significance of exudates after pneumothorax depends on their toxicity. An exudate causing no fever may be beneficial as the compression is made more complete. There are certain permissible and doubtful indications for pneumothorax. Certain indication is furnished by severe unilateral affection with absent or slight adhesions and soundness of the other lung. Permissible indications are severe affection of one side with fresh adhesions, severe affection of one side and slight affection of the other, severe affection of one side without adhesions, with protracted hemorrhage, severe hemorrhage of one side, the other lung not being involved too much, and slight involvement of one side which has resisted all other treatment. Doubtful indication is the severe involvement of one side and involvement of the lower lobe of the other lung. Contraindications are extensive disease of the better lung, extensive and firm adhesions of the side to be treated, serious complications in other organs, and caseous pneumonia of the affected side. Poorly managed pneumothorax is worse than none at all. Extrapleural thoracoplasty must be considered when firm adhesions make pneumothorax induction impossible. While it is a more serious procedure the lasting results are better in the severe cases. The cavities clear up and connective tissue proliferation occurs. The indications are evident failing of the patient's health without operation, unilateral involvement or good function in the other lung, adequate general condition, and impossible or insufficient pneumothorax. Success depends on the condition of the lung involved. If there is sufficient healthy tissue to ensure elastic compression, results are excellent. The main requisite of this operation is timely performance rather than its being resorted to as *ultimum refugium.* It is almost always advisable to perform it in two stages, especially in weakened patients. Tuffier originated the filling of cavities with lipomatous tissue. Bar introduced paraffin as filling material. Jessen filled ten cases with paraffin, and found that in a number of them the fillings were ejected aseptically. As to pleurolysis, its disadvantage lies in the fact that in the cases where it is most urgently needed it frequently is not successful. Because there are cases which are not sufficiently influenced, either by intrapleural pneumothorax or by thoracoplasty, Jessen proposes extrapleural pneumothorax with resulting fistula which remains open indefinitely, in order to prevent reëxpansion of the lung. It may be recommended in certain exceptional cases. By cutting the phrenic nerve Stürtz intended to put the involved lung at rest. While phrenectomy may produce a paralysis of the corresponding half of the diaphragm, its effect on the lung is only slight. It may be used as a supplementary procedure but in general is not very effective. From the nature of tuberculosis it is to be expected that operative success is not so uniform as in healthy individuals. But it is certain that operative treatment helps and even cures many patients who would die without it. It does not obviate the search for other remedies. The expectation of the future lies in the combination of climatic and immunizing treatment with operative procedures. The internist and the general practitioner must recognize the right time for operation.—*Die operative Behandlung der Lungentuberkulose, F. Jessen, Leipzig, 1921, Verlag von Curt Kabitzsch.*

Cauterization of Adhesions in Pneumothorax.—Of 40 cases in which cauterization was performed, 30 had a satisfactory result. Complete or sufficient compression of the lung was obtained in 27 out of 37 cases, which had adhesions to the apex and the lateral chest wall, as well as in 3 cases of adhesions to the diaphragm. From these 30 cases 4 must be deducted in which the operation was followed by a serous pleurisy or a tuberculous empyema, with serious consequences to the patients. In 26 out of 40 cases, therefore, a satisfactory pneumothorax was obtained and the operation was of genuine benefit. It would naturally be of interest to see whether the permanent results would be better in these cases than in pneumothorax cases in which this operation was not performed, but as yet there are not sufficient statistics for such a comparison. The immediate effect of cauterization justifies the operation as an adjunct to the pneumothorax treatment of pulmonary tuberculosis. As to the indications and contraindications, the string and membrane-like adhesions are best for the operation. Broad bands of adhesions are also suitable to a certain extent, but nothing can be said with certainty in advance as to the prospect of success. In 4 cases of the latter variety cauterization was done in two sittings, and it is quite possible that the use of the method can be extended in this way.—*The Cauterization of Adhesions in Pneumothorax Treatment of Tuberculosis, H. C. Jacobaeus, Surg., Gynec. & Obst., June, 1921, xxxii, 493.*

Management of Pleural Effusions in Therapeutic Pneumothorax.—*Summary*: The immediate effects of serous effusions occurring during pneumothorax treatment are usually beneficial; but ultimately they cause premature reëxpansion of the lung and obliteration of the pleural cavity. Therefore it is unwise to discontinue the treatment and adhere to the dictum of "leave effusions alone." Small, transitory effusions which do not alter the intrapleural pressure require no special attention. Moderate effusions which do not displace the mediastinum and do not interfere with the continuation of the pneumothorax need not be aspirated, but the pneumothorax should be continued with increasing intrapleural pressure to prevent obliteration of the pleural cavity. Large effusions should always be aspirated and replaced by air and the pressure regulated according to the needs of the individual case. Purulent effusions should always be aspirated and replaced by air, not only because of their toxicity,but also on account of their tendency to produce extensive adhesions and obliteration of the pleura.—*Management of Pleural Effusions in the Course of Therapeutic Pneumothorax, B. P. Stivelman and J. Rosenblatt, J. Am. M. Ass., July 2, 1921, lxxvii, 12.*

Two Cases of Surgical Thoracic Tuberculosis.—In the majority of cases closed operations are followed by excellent results. But in some cases the lesions are so diffuse that more extensive open intervention is preferable. Two cases of this sort are reported. A young man of twenty presented a large tumor on the left side of the chest, indurated but not fluctuating. Puncture yielded a small quantity of stringy pus mixed with blood, which passed with difficulty through a large needle. Four days later, aspiration was again attempted, this time yielding no pus. Because of the difficulty in emptying the abscess and its rapid extension, operation was decided upon. The purulent mass was found to be located under the pectoralis major, which was indurated, lardaceous and infiltrated with bluish granulations. The same condition was found in the pectoralis minor. The abscess was opened and the two muscles resected. Bone and cartilage were not involved. Calot's fluid was injected nine days later, and the wound was found to be cicatrized two weeks later. There is no notable impediment of the movement of the arm. The second case concerns a man forty-eight years of age, whose left hemithorax had become enlarged and painful. No concomitant lung tuberculosis was found. Fistulae, discharging a great deal of pus, and the general condition grew steadily worse. At operation, the infiltrated tissues were resected, including the costal cartilages which contained numerous abscesses. The left border of the sterum was carious and friable, but osteitis involved practically the entire sternum, which was therefore removed, except the healthy manubrium. Almost all the left costal cartilages were also removed, leaving the pericardium bare. Improvement was marked. Suppuration persists, but to a much smaller degree. Undoubtedly both cases were markedly benefited by the operation.—*Deux cas d'intervention large pour tuberculose thoracique (ablation du grand et dn petit pectoral, résection du sternum), L. Moreau, Progr. Méd., April 23, 1921, no. 17, 181.*

Antagonism Between Different Parts of the Spectrum.—Results obtained by ultraviolet light can be diminished if the proportion of red or infrared rays is increased without changing the intensity of the ultraviolets. Raw cotton is bleached when exposed to the quartz mercury light, but when solar rays or the infrared or visible rays or ordinary electric rays are added, the bleaching process can be stopped or become slower. A skin erythema induced in five minutes by the quartz mercury lamp will require seven minutes if infrareds or a sufficiently powerful light are added. Fluorescent effects on sulphides produced by ultraviolet radiation occur only with wave lengths greater than the orange; shorter wave lengths are reinforced. The antagonism between divisions of the spectrum is difficult to demonstrate with sensitized papers or even photographic plates.—*Phénomènes d'antagonisme entre diverses radiations (ultraviolet, spectre visible, infrarouge), H. Pech, Compt. Rend. Acad. d. Sc., 1920, clxx, 1246.*

The Action of the Ultraviolet Rays on the Cell.—The action of ultraviolet rays on the sea urchin's eggs can be summed up as follows: The rays affect the protoplasmic layer by coagulating the colloids and augmenting its permeability. The surrounding ions during the penetration precipitate the colloids and proteins of the cytoplasm which surround the colloidal droplets and the lecithins. These, then becoming free, unite to form a hyalin mass. This hyalin mass is decomposed and gives origin to a base (cholin?). This, increasing the decomposition, sets free the OH ions, which provoke a swelling by imbibing the colloids and proteins of the cytoplasm up to complete disintegration of the cell.—*Sur le mécanisme de l'action des rayons ultraviolets sur la cellule, S. Tchabotine, Ann. de l'Inst. Pasteur, May, 1921, xxxv, 321.*

The Use of Ultraviolet Rays in the Preparation of Vaccines.—Emulsions of typhoid and chicken cholera bacilli were prepared with sterile saline solutions, filtered through sterile paper, exposed for twenty minutes to ultraviolet radiation and inoculated into guinea pigs, 1 cc. for every injection. Injections were repeated three or four times at intervals of five days. Controls were carefully carried out. The conclusion was reached that the radiations rendered the cultures harmless without causing a loss of vaccinating property. One inoculation of a culture rendered the guinea pig immune to infection.—*Sull' uso dei raggi ultraviolетti nella preparazione dei vaccini, R. Lanzilotta, Ann d'Ig., 1920, xx, 245.*

The Influence of X-rays on the Development of Tuberculosis.—Guinea pigs were exposed to massive doses of X-rays, then inoculated on the following day intraperitoneally with cultures of tubercle bacilli. There was no difference between the time of the appearance of the disease in the rayed animals and that in the controls. In another series in which a second exposure was made several days after the first radiation, death occurred almost at the same time as in the controls. Another series in which two exposures were made before inoculation showed no variation. There was no marked difference in degree at postmortem between the lesions in the exposed animals and the controls. However, exposure to X-ray did show a marked metabolic effect by producing a rapid loss of weight, and also a great decrease in the number of leucocytes and the percentage of lymphocytes, which was more noticeable as the radiation was prolonged. The epithelioid cells and large mononuclears were normal, allowing the inference that these cells did not originate from lymphocytes.—*Influence de l'exposition aux rayons X sur l evolution de la tuberculose, J. Weinberg, Schweiz. med. Wchnschr., 1920, i, 14.*

Universal Light Baths in Ophthalmology.—Six years experience at the Finsen Institute, in treating about 200 patients with diseases of the eye and lupus, has taught the author that only conservative claims can be made for this method of treatment. The source of light was the carbon arc lamp. The periods of exposure, beginning with fifteen minutes, reached two hours. The conditions treated were phlyctenular conjunctivitis, keratitis, scleritis, diseases of the lachrymal passages, chronic iritis and iridocyclitis. All had been previously treated with the usual local applications and the only change was the inclusion of light baths. Only in tuberculous scleritis and iridocyclitis did these general radiations accomplish beneficial results. Rapid vascularizing was detected in most cases. It was suspected that phlyctenules were even provoked by the treatment. The baths can stimulate focal reactions which are analogous to those produced by tuberculin. Young patients responded better than older ones.—*Det universelle Lysbad i Ophthalmologien, K. Lundsgaard, Hosp. Tid., 1920, lxiii, 849.*

X-Ray Treatment of Laryngeal Tuberculosis.—The results are favorable but not conclusive. Some cases offered great encouragement and others made the author sceptical. The wisest procedure appeared to be to employ the cautery first, to eliminate the diseased tissue, and then to prevent recurrence by X-ray exposures.—*Über Röntgenbehandlung der Kehlkopftuberkulose, C. Kümmell, Verhandl. d. Gesellsch, deutsch Naturf. u. Ärzte, 1920.*

Treatment of Laryngeal Tuberculosis with the Arc Light.—Patients, lying down and stripped, were exposed to four carbon arcs of twenty ampere current, first for fifteen minutes, in the second week for thirty minutes, and so on until one hour was reached daily. Treatment was continued for many weeks and months. Of 74 really severe cases, 3 were healed, 35 improved, 6 uninfluenced, and 16 became worse while under treatment. Almost all had second stage pulmonary tuberculosis. Especially good were the results with ulcerations and edematous swellings in the interarytenoid space. Silence treatment was also carried out. With the larger infiltrations the cautery was also employed, as well as other surgical procedures. In one group, the laryngeal condition was favorably influenced, while the pulmonary and general condition became worse. No method offers better results for laryngeal tuberculosis than the combined employment of carbon arc radiation with local surgical treatment.—*Behandlung der Larynxtuberkulose mit universellen Kohlenbogenlichtbädern, N. R. Blegvad, Deutsche med. Wchnschr., 1920, lxvii, 621.*

X-Ray Treatment of Pulmonary and Intestinal Tuberculosis.—The problem of X-ray treatment of pulmonary tuberculosis is chiefly one that involves the knowledge of the anatomy of the lesion and the employment of proper dosage. The X-ray works only on tuberculous granulation tissue and the treatment is suited only for slowly progressive and stationary types, as well as for nodular and cirrhotic types; it merely helps along the natural healing tendencies. The technique must be suited to individual cases, varying the dose and the intervals. Larger doses and shorter intervals are employed particularly in bronchial and lymph node tuberculosis and the more favorable pulmonary cases; smaller doses and larger reaction periods in the progressive cases. The author shows many X-ray plates to demonstrate the fibrosing effect of the X-ray. It is necessary to employ this treatment in a sanatorium under careful supervision. The results with intestinal tuberculosis have proved very favorable.—*Die Behandlung der Lungen- und Darmtuberkulose mit Röntgenstrahlen, A. Bacmeister, Verhandl. d. Gesellsch. deutsche Naturf. u. Ärzte, 1920.*

X-Ray Treatment of Peritoneal Tuberculosis.—Excellent results were obtained in all cases of tuberculous peritonitis without ascites, but with marked adhesions, regardless of the involvement of the genital organs. Operative intervention gives bad results. After an exploratory laparotomy in the miliary type with ascites, the treatment was also valuable. If the serosa alone is involved, it is wiser to spare the genital organs from the exposure, by radiating merely the abdomen front and back, excluding the small pelvis. Exploratory laparotomies are of great advantage in protecting the ovary which one desires to keep functioning, even when the adnexa are involved.—*Strahlentherapie für Peritonealtuberkulose S. Stephan, Monatschr. f. Geburtsh., u. Gynäkol., May, 1921, liv, 314.*

X-Ray Treatment of Peritoneal and Genital Tuberculosis.—Six cases are reported from the Greifswald clinic as completely healed. Peritoneal cases with tumor formation, but without ascites, and those in which there is marked cachexia are especially suitable. Operation, together with X-ray treatment, is indicated in the ascitic-miliary form. The same indications hold good when there is a combination of peritoneal and genital tuberculosis. Even the severe forms of genital disease with large pus foci are rayed.—*Zur Röntgenbehandlung der Bauchfell- und Genitaltuberkulose, S. Stephan, Strahlentherapie, 1920, x, 957.*

Heliotherapy in German Sanatoria.—This booklet is published as a result of questionnaires sent to the various sanatoria of Germany. It summarizes the cumulative evidence in regard to the value of sunlight, artificial light, the air bath, the X-ray and the incandescent light in the treatment of tuberculosis. In addition to this, the treatment of chronic otitis media with artificial sunlight, the combined use of quartz light and the X-ray, and the specific results of ultraviolet radiation in the Institute of Lostau are taken up in detail. With sunlight, Rollier's technique of graduated exposure, and the opinion of many workers in regard to the particular indications for this mode of treatment, are given. With artificial light, the many lamps used abroad are considered from the standpoint of employment of the individual parts of the spectrum. The results at Lostau together with many theories of the manner in which light accomplishes results are considered with particular reference to the value of pigment, but no uniform conclusion can be drawn. The effect of the mercury quartz light on the body physiology is also considered, offering many contradictory viewpoints.—*Die Lichtbehandlung (Heliotherapie) in den deutschen Lungenheilanstalten, G. Liebe, Beitr. z. Klin. d. Tuberk., 1919, Supplement Band, viii.*

Light, Skin and Tuberculosis.—The writer is particularly interested in placing light as a therapeutic agent upon a strictly scientific basis; but the results thus far are not as good as the effort would seem to deserve. When one refers to light, only the ultraviolet spectrum is meant in many cases. The ultraviolets that penetrate through the upper layers of the skin are almost always absorbed in the basal cells. The inner organs are affected indirectly by means of the action on the basal cells. The theory is offered that light returns to the skin its natural properties. It protects the skin that is otherwise anemic and substitutes a physiological hyperemia. Tuberculosis is influenced indirectly and not in any specific way. General improvement occurs indirectly through the stimulation of the inner secretory functions of the basal cells.—*Licht, Haut, Tuberkulose, H. Jesionek, Fortschr. d. Med., 1920, no. 11, 213.*

Light and Climatic Treatment of Tuberculosis.—The specific action of light treatment depends on ultraviolet rays which are present in much smaller numbers in the lowlands than in either highlands or in artificial sunlight. This is so for general as well as for local radiations. The best rays for a strong irritation to affect sluggish wounds are the short ultraviolets, below 300 millimicra, which are particularly present in the ultraviolet lamp. The best rays to produce hyperemia are the more penetrating ultraviolets above 300 $\mu\mu$ in combination with the warm rays that are present in sunlight and in various lamps. It is important to interrupt the treatment at times to prevent the skin from becoming accustomed to the light. Change of climate is at times also important.—*Zur natürlichen und künstlchen Sonnen- und Klimabehandlung der Tuberkulose, H. Bach, Deutsche med. Wchnschr., 1920, xlviii, 795.*

Chaulmoogra Oil in the Treatment of Tuberculosis.—The similarity in morphology and staining characteristics of leprosy bacilli and tubercle bacilli, and the specific action of chaulmoogra and its related oils on the acid-fast group of bacteria, furnish a scientific basis for using them in the treatment of tuberculosis. The acid fractions of chaulmoogra oil, obtained by the method of Hollmann and Dean and modified by Aldrich, were used in the following experiments. Forty-eight guinea pigs were divided into 5 groups: (1) 12 pigs were inoculated with human type tubercle bacilli and left without further treatment as tuberculous controls; (2) 12 pigs were similarily inoculated and divided into groups of 3 each, which were given introperitoneal doses of the acid sodium salts of the four fractions, A, B, C and D, of acids of chaulmoogra oil; (3) 8 pigs were left as entirely untreated controls; (4) 12 nontuberculous pigs received the same treatment as the tuberculous pigs of group two; (5) 4 pigs received increasing amounts of the A, B, C, and D fractions in a toxicity test. This report is described as preliminary; but the following findings are given: One per cent solutions of the acid sodium salts of the four fractions are least irritating and are readily absorbed from the peritoneum. No pathological findings could be attributed to the drug. On the other hand it seemed to cause an increase in weight. A bactericidal action on tubercle bacilli in 1:10,000 dilution was found. Of the 12 pigs inoculated with tuberculosis and not treated all died except one. Of the 12 treated tuberculous pigs only one died of the disease. The others were killed for comparison, one whenever a tuberculous nontreated pig died. A marked difference in pathological findings was observed, the advantage being in favor of the treated pigs. Treated pigs showed an average gain of weight of 49 gms. over the ones not treated. —*Chaulmoogra Oil in the Treatment of Tuberculosis, W. S. Culpepper and Marjorie Ableson, J. Lab. & Clin. Med., May, 1921, vi, 415.*

Tuberculin in Epilepsy.—Epilepsy is considered by some a contraindication to the administration of tuberculin. Crocket's experience shows, however, that it is a decided indication, especially in the presence of an active or quiescent tuberculous lesion, and when there is a family history of tuberculosis. He began to give tuberculin six and a half years ago to a patient thirty-two years of age, who had suffered from epilepsy of the major type since the age of seven, and who had a large mass of tuberculous lymph nodes below the right ear with several discharging sinuses. In the course of a year and a half the glands disappeared entirely. With the disappearance of the tuberculous lesions, the epileptic fits became fewer, and after two and a half years ceased entirely, and the patient also improved mentally. For four years this patient has been free from both tuberculosis and epilepsy. About eighteen months ago the author began to administer tuberculin to several other epileptics who had no clinically obvious tuberculosis, but gave a family history. One of these responded very well. Tuberculin was first given to him in November, 1919. For nearly fourteen months he has had no signs of epilepsy and has also improvd mentally. Five others to whom tuberculin has been given for six to twelve months show a diminution in the number and severity of their seizures. Three show no change. General reactions have been avoided, but once or twice local reactions of a rather severe type occurred when large doses of bacillary emulsion were given. On two occasions cold abscesses formed, which had to be aspirated.—*Tuberculin in Epilepsy, J. Crocket, Brit. M. J., March 26, 1921, no. 3143, 458.*

Tuberculosis of Tonsils.—*Conclusions*: 1. The systematic search of a limited number of microscopic sections, so orientated as to show in each the entire surface of a vertically bisected tonsil, is the only practicable routine method for detecting tonsil tuberculosis. 2. The incidence of active tonsil tuberculosis in a series of 8697 consecutive cases was found to be 2.35 per cent. This minimum figure would have been increased by an unknown, but probably small, amount if it had been possible to examine all portions of each tonsil. 3. The incidence in respect to sex shows tonsil tuberculosis to be slightly more common in females than in males at practically all ages. 4. In the series of 204 positive cases here reported, the range of ages was from two to fifty-nine years. The incidence in various age groups depends largely on the character of the population from which the material is derived, the incidence being particularly high in institutions for the care of children and among medical students, internes and nurses. 5. Tonsil tuberculosis may be divided into three types: focal crypt infections, ulcerative lupus-like lesions and diffuse miliary tuberculosis. 6. The crypt infection is the most common type, is usually unilateral, involves one or more crypt areas only, and avoids the lymph follicles. Some of these cases are autoinfections in open respiratory tract tuberculosis but the majority must be considered cases of primary focal tonsil tuberculosis. 7. The ulcerative lupus-like lesions result from the coalescence of crypt infections at the mouths of crypts or from direct extension from neighboring surfaces. 8. The diffuse miliary tuberculosis is usually a bilateral, or, if the pharyngeal tonsil is examined, a universal tonsil lesion. The tubercles are widely scattered and occur almost exclusively in the follicles and germ centres. This type can best be explained as a hematogenous miliary dissemination. 9. Mixed types occur as in patients with open pulmonary tuberculosis, in which autoinfection may be associated with hematogenous miliary tuberculosis, giving a combination of crypt infections with diffuse miliary tubercles.—*The Incidence and Histopathology of Tuberculosis of the Tonsils, C. V. Weller, Arch. Int. Med., June, 1921, xxvii, 631.*

Laryngopulmonary Tuberculosis.—Tuberculosis of the larynx is always secondary to tubeculosis of the lungs or lymph nodes. For this reason the prognosis is grave. In those cases where the trouble in the larynx has been cured by local treatment, the pulmonary lesion was either slight or inactive. Laryngeal tuberculosis should be spoken of and treated as laryngopulmonary tuberculosis. Except in the cases where the pulmonary lesion is inactive or distressing symptoms must be relieved, patients should not be treated in the office or clinic. Tuberculosis of the larynx is almost invariably found among tuberculous adults, and occurs in about 25 per cent of the patients. It is present only in those cases which have, or have had, a positive sputum. Usually there is a predisposing cause, such as nasal obstruction, chronic pharyngitis, tonsillitis, catarrhal laryngitis, history of excessive cough, excessive use of tobacco and alcohol, and lues. The infection is caused directly by the tubercle bacilli implanted on the mucous membrane of the larynx. In almost every case there is an open pulmonary lesion which means a constant stream flowing over and bathing the laryngeal mucosa. There are three types of laryngeal tuberculosis: acute, subacute, and chronic. The acute type is characterized by a soft edema of the larynx with a marked tendency to ulceration. The patient usually suffers from hoarseness, a sensation of fulness in the throat and irritation with a constant desire to cough and expectorate. Dysphagia may be pronounced. With the patient in good general condition, the disease may run its course, become subacute and occasionally arrested, but in general the lesion is hardly amenable to treatment. The patient, as a rule, dies in from six to eighteen months. The subacute type is characterized by a pseudo-edema of part or parts of the larynx with a moderate tendency to fibrosis. Hoarseness and dryness in the larynx are the symptoms complained of; and the patient is usually benefited by treatment. The prognosis is favorable when the general condition of the patient is good and an early diagnosis of the disease has been made.

The chronic type gives the best prognosis and is characterized by firm infiltration of part or parts of the larynx with a marked tendency to fibrosis and healing. The larynx should be examined in every tuberculous individual, so that early involvement may be discovered. Examination of the respiratory tract should begin with the nasal chambers. In making a diagnosis care must be used to distinguish between bronchiectasis, accessory sinusitis, laryngitis sicca, and lupus. In the chronic cases the voice may remain affected while the prognosis for life is good. Patients with the most extensive lesions do not give the poorest prognosis. It is not so much the extent as the character of the lesion that determines the gravity of the individual case. Temperature, pulse and weight constitute the keynote to the patient's general condition. Underlying disease, such as syphilis, aggravates the prognosis by lowering the general vitality of the patient. The economic condition is an important factor. Ample financial resources are necessary to cover an average period of three to five years. The patient of independent means, who is faithful to treatment, offers a better prognosis than one who must earn his livelihood or return to work after a brief course of treatment. Prognosis as to voice is more definite. It depends upon the extent, location and character of the local lesion. Cases with involvement of the true cords and interarytenoid space give a poorer prognosis than if situated elsewhere in the larynx. Treatment is general, prophylactic and local. The lungs should first receive attention and absolute rest in bed must be insisted upon, before any attempt is made to treat the larynx. Outdoor sleeping should be urged and a generous diet prescribed. Predisposing factors, capable of producing a catarrhal condition of the larynx, are to be removed. Rest of the voice is imperative. For relief of pain, orthoform or cocaine before meals may be given. Epiglottidectomy is sometimes necessary, and always indicated where the lesion is limited to the epiglottis and the patient's condition permits.—*Laryngopulmonary Tuberculosis, J. Dworetzky, Med. Rec., July 9, 1921, c, 57.*

Nerve Block in Laryngeal Tuberculosis.—The successful injection of an anesthetic solution into the sheath and substance of the internal laryngeal nerve produces a block anesthesia of the areas supplied by the terminal filaments of the nerve. This procedure is easily carried out. The pain secondary to injection is accentuated for a few seconds, after which much relief is experienced. The block anesthesia lasts for a period of at least ten days and is complete. When the injection has been made in the tissue around the nerve, then only an imperfect anesthesia is obtained, of a maximum duration of four or five days. After nerve block any local procedure is carried out with greater ease. The patient can swallow and speak with a clearer voice. It is surprising to see how much weight an emaciated tuberculous indivdual may gain after ten days anesthesia of the larynx. Nerve block of the internal laryngeal nerve, topical applications of cleansing solutions and of formaldehyde in increasing strength, the judicious use of tuberculin, and general hygienic measures will contribute to marked improvement and alleviation of symptoms.—*Block Anesthesia of the Internal Laryngeal Nerve, A. Wallace, Southwest. Med., July, 1921, v, 16.*

Nontuberculous Enlargement of the Bronchial Lymph Nodes.—Gähwyler calls attention to seven cases in which the roentgen ray and all the physical findings point to tuberculous disease of the bronchial nodes, with pains between the scapulae, and ready fatigue, etc. But the persisting good general health and other features of the cases seem to disprove absolutely a tuberculous affection, and tuberculin tests have been constantly negative for years. The patients are five children between six and sixteen, a woman of thirty-five, and a physician of thirty-eight. Nageli's figures as to the prevalence of tuberculosis need revision, as he classified as tuberculous all calcified nodes found in cadavers. The roentgen ray findings are unable to differentiate tuberculous from nontuberculous calcification.—*Über nicht-tuberkulöse Bronchialdrüsenschwellungen und Verkalkungen, M. Gähwyler, Schweiz. Med. Wchnsckr. April 7, 1921, 317.*

The Heart and Tuberculosis.—*Summary;* An electrocardiographic study of 97 patients with pulmonary tuberculosis in the Montefiore Hospital (N. Y. City) revealed 29 per cent with right ventricular predominance, 30 per cent with left ventricular predominance, and 41 per cent with no predominance of either chamber. Right ventricular predominance is not always associated with any particular type of tuberculosis. It is found more commonly in young than in old patients, and twice as frequently in men as in women. Left ventricular predominance is not always associated with any particular type of tuberculosis. It is found more commonly in older patients and is twice as frequent in women as in men. Left ventricular predominan occurs more frequently with the increasing age of the patient. In contrast to the necropsy findings reported in the literature, right ventricular predominance is not found more frequently in association with fibroid phthisis, or with pleural adhesions, than with other types of pulmonary tuberculosis.—*The Right Ventricle in Pulmonary Tuberculosis, E. P. Boas and H. Mann, Arch. Int. Med., July 15, 1921, xxviii, 62.*

A Case of Tuberculous Mesenteric Nodes.—Apropos of two cases of tuberculosis of mesenteric lymph nodes recently reported by H. N. Clute, the writer reports a similar case. The patient was a male, aged twenty-seven, laborer, whose chief complaint was abdominal pain and vomiting. The family history was negative, and the past history negative except for influenza-pneumonia one year before. Attacks of epigastric pain accompanied by nausea and vomiting had been present for eight months. Physical examination revealed a firm nodular tumor, the size of a hen's egg, in the left upper quadrant, to the left and above the umbilicus; and a smaller freely movable one just at the right of the larger mass. The temperature and pulse remained normal. The white blood count was 12,000. X-ray of the lungs showed marked increase in density and mottling in both apices. On operation, a large firm mass of mesenteric nodes in the region of the transverse colon was found. The mesentery was studded throughout with enlarged nodes. No attempt at removal was made. From the location of the tumor and its fixation a pancreatic tumor of some kind had been diagnosed.—*A Further Case of Tuberculous Mesenteric Glands, J. M. Lynch, Boston M. & S. J., April 14, 1921, clxxxiv, 384.*

Bone Tuberculosis.—Material, collected during the treatment of 50 cases of bone tuberculosis, was studied from a clinical standpoint. The cases presented various types of the manifestations usually associated with infectious bone lesions. The symptoms and physical data established the tubercle bacillus as the etiological factor without great difficulty. In some cases, diagnosis of tuberculosis was not made certain until the material obtained at operation was sectioned and studied microscopically, and animal inoculation had confirmed it. The pathological process was not found to be essentially different, wherever it may occur. If tissues are involved that possess the property of rapid proliferation when infected, this process will be observed when the tubercle bacillus is the agent; but if tissues are involved which do not rapidly proliferate destruction will occur. The tuberculous process, as it affects bones and joints, is one and the same; variations are due only to the characteristics of the tissue infected. But it is unwarranted to classify this disease according to the type of reaction observed. Such terms as infiltrating, atrophic, caseous and hypertrophic tuberculosis of the bone, or chronic synovial tuberculosis, and fungating or granulating tuberculous synovitis, are not apt. This series of 50 cases points to the fact that the disease is primarily osseous.—*Tuberculosis of Bone: Results of a Study, N. Allison, Arch. Surg., May, 1921, ii, 593.*

Tuberculous Hip Disease and Its Simulants.—In the Frediksvern (Norway) Coast Hospital, in the period from August, 1903, to June 30, 1918, 252 skiagrams of the hip joint were made. Every case showing destructive processes of the joint, with or without suppuration, was regarded as tuberculous, unless proved otherwise by tuberculin test or pathological examination. In 19 of the 262 cases, signs of disease were lacking or were so slight that a definite diagnosis was impossible. Of the 243 positively diagnosed cases, 171 were tuberculous, leaving 29.6 per cent nontuberculous. The percentage of nontuberculous hip affections is still further decreased if only the seven year period of July 1, 1911, to June 30, 1918, is considered, during which the author personally investigated and treated every case. During this period 613 cases were admitted with a diagnosis of tuberculosis of the hip, but this diagnosis was confirmed in only 64 cases, the proportion of nontuberculous cases being 43.4 per cent. Most of the nontuberculous cases in both groups were diagnosed as Calvé-Perthe's disease. In 13 of the cases it was impossible to establish a diagnosis even after reëxamination. In 12 of them tuberculosis could be definitely excluded; in the one remaining case there was a history of tuberculosis of the elbow, but the X-ray examination of the hip was negative, and treatment caused no change in either the clinical signs or the X-ray picture. The child remained in good general health, the only symptoms of hip disease being atrophy of the gluteal muscles and a marked limp. When the cutaneous test is positive, signs of hip disease, however slight, call for treatment for tuberculosis until the X-ray picture or the subsequent course of the disease definitely excludes the diagnosis. *Conclusions:* 1. Tuberculosis of the hip is less common than was once supposed. 2. All statistics dealing with the results of treatment of this disease up to the present time are worthless. 3. If most of the benign cases be excluded from these statistics, the prognosis for true tuberculosis of the hip will be found to be far worse than was formerly supposed. 4. In spite of modern diagnostic methods, it is impossible in about 10 per cent of all cases of hip disease to establish a diagnosis.—*Tuberculous Hip Disease and Its Simulants, H. Sundt, Tubercle, April 1921, ii, 289.*

Tuberculosis of Knee Joint.—Knee joint tuberculosis constitutes about 20 to 25 per cent of all cases of joint tuberculosis. The disease may be primary in either the synovia or the bone. Shaft tuberculosis is rare. Knee joint tuberculosis must be differentiated from chronic synovitis due to sprains, trauma or infection as well as from syphilitic joint affections, sarcoma, carcinoma, etc. In children there is a more marked resistance to the disease and reparative processes are much more active than in adults. For this reason, conservative treatment such as rest and immobilization are indicated in children. Operative procedure hastens and insures a cure and is therefore indicated in adults. The operation is that of resection of the knee. The author follows the technique of R. H. Hibbs, in that only the cartilages of the articulating surfaces of the femur and tibia are removed. There is no attempt to excise or remove the capsule. The patella is excised subperiosteally and placed in a bed chiselled out in the femur and tibia, thus both fixing the bones and acting as a bone graft. Then the joint is immobilized in a plaster cast for three months, by which time firm union is to be expected.—*Treatment of Tuberculosis of the Knee Joint, J. J. Kurlander, Ohio State M. J., January, 1921, xviii, 20.*

Tuberculosis of the Skin.—Lupus vulgaris, or true tuberculosis of the skin, may be the sequel of inoculation from within or from without. If from within, the lesions are apt to be widespread; if from without, localized. Often they are adjacent to a focus of visceral tuberculosis and show evidence of extension by contiguity. Tubercle formation is the essential feature, with subsequent caseation, necrosis, and attempted healing. If the organism is of low virulence and the tendency to heal is marked, the tuberculous lesion is nonulcerative and involutes, leaving a thin papery scar. If the virulence is considerable and the resistance low, an ulcerative lesion develops which may produce extensive destruction, especially when it occurs about the mucocutaneous borders. The scar of lupus vulgaris is markedly contractile, apt to be tough and banded, and usually produces distortion. Inoculation tuberculosis of the skin is most familiar in the form of tuberculosis verrucosa cutis, the warty papule or plaque with a rough, horny surface and an erythematous areola. Lesions of this type usually occur on surfaces exposed to trauma and are not uncommon about the finger nails. There is a type of inoculation tuberculosis which produces, at the site of inoculation, a trivial reaction in the form of a dozen or more tubercles, sometimes with a slight tendency to ulceration and prompt central healing. The infection quickly metastasizes to the regional lymph nodes, producing there an immediate suppurative reaction with sinus formation. By the time the regional lymphatic process is fully developed the original focus may have all but disappeared. Lupus erythematosus is classed under tuberculosis of the skin, but is not a true tuberculosis, though associated with it. It is characterized by an inflammation of the follicles with the formation of adherent conical, horny plugs. The coalescence of these hyperkeratotic plugs forms the adherent scale. The sequel of the follicular inflammation is the atrophy so characteristic of the disease. Erythematous lupus about the face and in the scalp is most disfiguring, although it is seldom a serious condition. When it appears on the hands it must be regarded as a transition towards the grave and often fatal toxic form of lupus erythematosus disseminatus. Ordinary cases have been known to respond to the administration of tuberculin by developing the fulminating disseminated type with hyperpyrexia and death. For that reason tuberculin should not be used in the diagnosis or treatment of lupus erythematosus. Treatment in any form is unsatisfactory. The use of the X-ray or radium on either lupus vulgaris or lupus erythematosus is to be discountenanced, because of the grave risk of rapid malignant degeneration. Transitions from erythematous lupus into the sarcoids are not infrequent. Lichen scrofulosorum belongs, in all probability, to the toxic manifestations in the skin produced by visceral tuberculosis. The essential lesion is follicular, a pale yellow papule forming about the mouth of the hair follicle, and a spinous plug usually appearing in the mouth of the follicle. These lesions are grouped into patches, the gross appearance suggesting goose flesh. In papulonecrotic tuberculids the essential lesion is a papule, inflammatory in character, which within a few hours of its appearance develops a central vesicle or softening, associated with a necrosis of the involved tissues. This central necrosis dries down to form a hard, dark, conical, plug. When this plug is detached in the process of healing a scar persists. Papulonecrotic lesions may occur on any part of the body. The association of papulonecrotic tuberculids with foci of tuberculosis is practically beyond dispute. An equally interesting association of these lesions is that with foci of septic infection. Rheumatism and tonsilitis run parallel with pneumonia and influenza in the symptomatic background of tuberculids. In the treatment of papulonecrotic tuberculids arsphenamin has given satisfactory results. A low or diminished resistance is a distinct contraindication to the use of the drug.—*Tuberculosis of the Skin in Some of Its General Medical Aspects, J. H. Stokes, Northwest Med., April, 1921, xx, 79.*

Is Lupus Erythematosus Due to Tuberculosis?—The question of the relationship of lupus erythematosus to tuberculosis was studied by estimating the percentage of clinical tuberculosis detected in patients with lupus erythematosus discoides; by searching for signs of tuberculosis in the records of patients with dermatoses ordinarily not associated with tuberculosis; by comparing the frequency of clinical tuberculosis in such dermatoses as erythema multiforme and erythema nodosum, with the incidence of tuberculosis in lupus erythematosus discoides chronicus; and by comparing the incidence of tuberculosis in the records of patients with tuberculids, with the frequency of tuberculosis in patients with lupus erythematosus discoides chronicus. It was found that that the incidence of clinical tuberculosis in dermatoses admittedly of nontuberculous origin (38.1 per cent) is approximately as high as in lupus erythematosus discoides chronicus (35.7 per cent). Clinical tuberculosis is no more frequent in dermatoses like erythema multiforme and erythema nodosum (32 per cent) than in lupus erythematosus discoides chronicus (35.7 per cent.) The frequency of clinical tuberculosis in patients with tuberculids (84 per cent) presents a striking contrast if compared with its frequency in lupus erythematosus discoides chronicus (35.7 per cent). The two lesions, therefore, cannot have the same pathogenesis. The tuberculous origin of lupus erythematosus discoides chronicus has not been proved by experimental work. Clinical observations, including this statistical study, seem to favor various etiological factors.—*Is Lupus Erythematosus Discoides Chronicus Due to Tuberculosis?—W. H. Goeckerman, Arch. Dermatol. & Syphilol., June 15, 1921, iii, 788.*

Chronic Nontuberculous Lung Disease.—In a recent article by Greeley and Brereton, an account was given of investigations into the bacteriology of the sputa of some thirty cases of chronic nontuberculous lung disease. They devised a medium (lactic acid-agar) which would act selectively in the cultivation of moulds. Upon this plants were made from various specimens, and cultures incubated at both body and summer (70°–80° F.) temperatures. It was found that the sputa of 14 of the cases contained the penicillium glaucum; 2 the mucor corymbifer; 1 the aspergillus fumigatus; while those of 13 cases gave (on culture) only yeast forms. Of the 30 some cases, 6 showed physical signs of lung infiltration. Six of these cases had been classed by their medical attendants as chronic bronchitis, 2 as acute bronchitis and 3 as bronchial asthma. The diagnosis of chronic nontuberculous lung disease was made, in the cases in question, as the result of numerous recorded sputum examinations for tubercle bacilli, which had resulted negatively; and by the finding of organisms (fungi) known to be capable of producing such lesions. After making a diagnosis of nontuberculous fungoid lung disease, treatment is greatly facilitated, since one is then free to push medication, as by the iodides, a procedure which would be dangerous in tuberculous lung disease. Besides this, autogenous vaccines may prove beneficial. Some idea of the effect of such vaccines can be had by reading the detailed report of 4 cases. A vaccine is only a stimulant to the natural curative powers and therefore results depend, not upon the injected material, but upon that which may be produced in response to its action. One must look to the reactions which follow an injection for indication that such production is under way, and the size of doses and intervals between them must be regulated according to the effects of previous injections. In such conditions as are under consideration it is suggested to start with a dose of 500 million organisms, and then at the end of three days consider the size and time of the next dose. If a distinct local reaction, with definite swelling and redness, follows the injection, this evidence of the desired stimulation renders it unnecessary to increase the dose at all, or certainly to not over 10 per cent. Reinjections should never be made until twenty-four hours after the subsidence of all reaction. This usually brings them around every three days; and the same interval had better be allowed when there is no reaction. Noticeable focal reactions (heaviness over the chest, increased or diminished cough and expectoration) and even constitutional manifestations, such as elevation of temperature, may occur, and indicate a maximum stimulation. Such reactions had better be followed by reduction in doses. In case no reaction is elicited, the next dose should be increased 25 per cent, and so on. In case a patient persistently fails to react, say, after the initial dose of 500 million has been increased tenfold, the administration of potassium or sodium iodide, to the extent of 15 to 30 grains a day, may be tried together with the vaccine, since it seems that iodine arouses the reactive mechanism. It is claimed that good results may follow vaccine treatment without noticeable reaction, but cases showing the latter certainly make the greatest improvement.—*Chronic Nontuberculous Lung Disease, H. Greeley, Med. Rec., July 16, 1921, c, 99.*

Bronchiectasis and Accessory Sinus Disease.—Patients with chronic bronchitis and bronchiectasis have often been classed as tuberculous and placed in tuberculosis institutions both before and since the war. They usually have a chronic cough with profuse expectoration, but without tubercle bacilli. If their noses and accessory sinuses were examined, these would frequently be found to be the seat of chronic suppuration. Appropriate local treatment benefits the chest condition. The authors advocate routine examination of the upper air passages in every such case and report three illustrative instances out of a series of thirty-eight.—*Bronchiectasis and Bronchitis Associated with Accessory Sinus Disease, G. B. Webb and G. B. Gilbert, J. Am. M. Ass., March 12, 1921, lxxvi, 714.*

Tropical Bronchopulmonary Mycosis.—The cases came to necropsy as the result of some intercurrent medical or other accident. Cultures from many lungs were taken in order to obtain a pathological picture, the result of a pure mycotic infection. On cut sections, the lungs resemble very much a tubercle infection. Although the blood supply is completely cut off from these filbert-like growths, yet there seems to be no necrosis, and it is possible that the surrounding tissues indirectly supply nourishment. As many different specimens have been examined without finding any lungs in which necrosis has taken place, it would seem that the fungi, at least those found in Siam, have in the beginning a stimulating effect on the tissue cells. In view of the fact that mixed infections of long standing present on postmortem examination the same firm connective tissue tumors, it is doubtful whether these growths, except under the most adverse conditions, break down. The acute cases as well as the chronic may be mild or severe, but the average case presents signs and symptoms not at all unlike those of an acute bronchitis. There is some fever, irritating cough, expectoration of large amounts of mucous or mucopurulent sputum and a general sensation of illness. The chronic cases, on the other hand, are to be differentiated from tuberculosis and spirochetosis. The symptomatology of an average chronic mycotic lung infection produces all of the signs and symptoms of a tubercle infection even to true hemoptysis, which would tend to show that these mycotic tumors do, under favorable conditions, break down and degenerate. A diagnosis can be made only after laboratory examinations. The prognosis and treatment of the chronic cases is not unlike that in tuberculosis. From a public health point of view the only difference between tuberculosis of the lungs and bronchopulmonary mycosis is one of degree. They are both contracted in the same way. They are both incapacitating, and are both preventable. It is not improbable that many cases of supposed tuberculosis of the lungs, especially in some of the southern states of the United States, would on careful bacterial examination prove to be cases of bronchopulmonary mycosis.—*Tropical Bronchopulmonary Mycosis, R. W. Mendelson, J. Am. M. Ass., July 9, 1921, lxxvii, 110.*

Epidemiology of Tuberculosis.—Opinion concerning the epidemiology of tuberculous diseases has changed enormously within the last decade. Bushnell states that there is a fundamental distinction between the epidemiological behavior of tuberculosis recently exposed to infection and amongst populations wherein the disease has prevailed for generations. Amongst acclimated races the mortality of tuberculosis varies with the hygienic conditions and social status. Any attempt to eliminate sources of infection in settled countries would be positively injurious, as the danger of a chronic and usually relatively benign infection would be exchanged for the danger of an acutely fatal one. Either physical, occupational selection, hygienic conditions of labor, or opportunity for massive infection, are important factors in etiology and must be called upon to explain the difference in mortality in the different industries.—*The Epidemiology of Tuberculosis, Editorial, Brit. M. J., April 16, 1921, no. 3146, 570.*

Congress of the German Society for Internal Medicine.—This, the thirty-third, congress of the society was held at

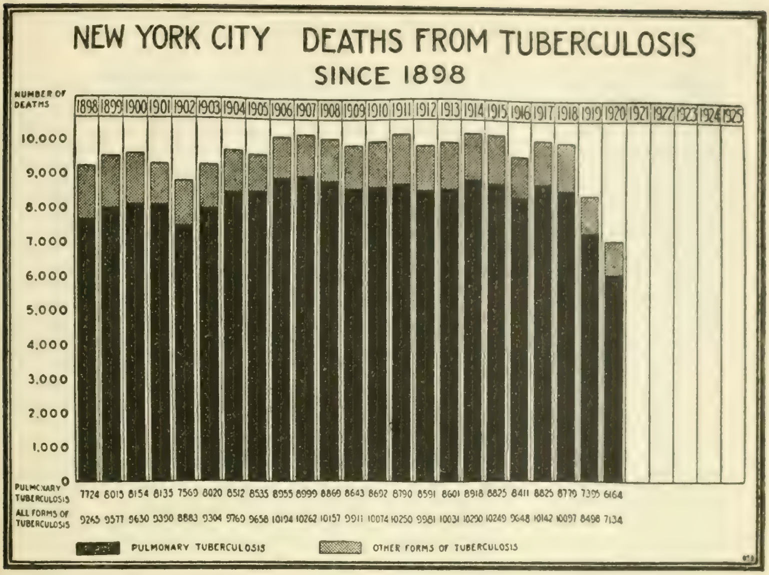
Wiesbaden, April 18–21, 1921. A symposium on the treatment of pulmonary tuberculosis formed the topic of the first day's discussion. Aschoff spoke on the natural healing tendencies in phthisis. He used the clinical term phthisis advisedly, whereas the clinicians clung to the old anatomical nomenclature. Uhlenhuth discussed the experimental basis of tuberculosis therapy. Animal experiments intended to prove the prophylactic and curative value of tuberculins, including the Deycke-Much preparation, have not stood the test of time. In man, tuberculin has achieved incontestable results. But these are not due to any antitoxic or antibacterial action, but to local hyperemia. It is an established fact that childhood infection imparts partial immunity. The bacillus should be the object of future therapeutic research. Chemotherapy may also hold out hope. Gerhardt and de la Camp spoke on bedside and X-ray treatment respectively. X-rays should be used only in cases tending to fibrosis. Only in minimal doses do they stimulate connective tissue formation. Brauer discussed the operative treatment with which his name is so intimately associated. In the general discussion, twenty men illuminated the present status of phthisiotherapy. Nothing new was brought out. With a strictly critical sense and apparently a feeling of resignation, the speakers concluded that we have not progressed much further in treatment than in the days of Brehmer and Dettweiler.—*Summarized by Prof. H. Kohn, Berl. klin. Wchnschr., April 25, 1921, no. 17, 435.*

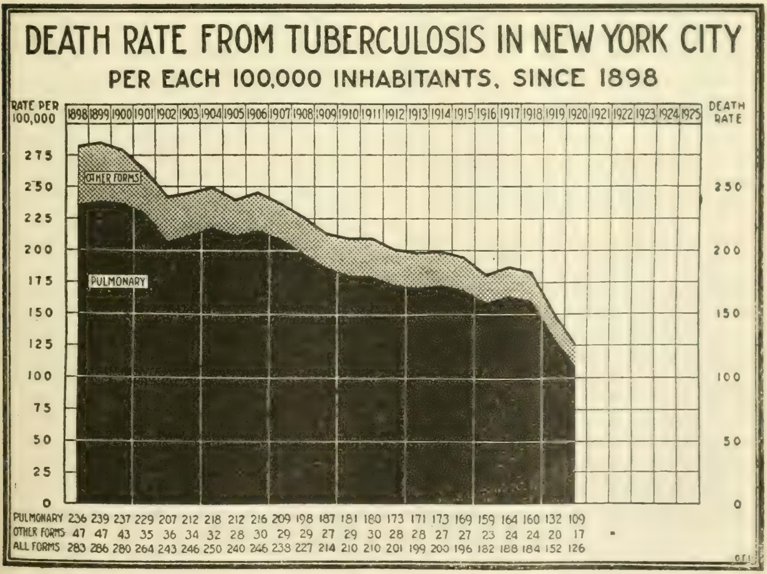
Tuberculosis: Retrospect and Prospect.—It may not be without interest to look back ten years and as best we can reconstruct our old modes of thought about tuberculosis, compare them with views to-day, and, perhaps even try to guess at some changes which to-morrow may bring. Of the many teachers in tuberculosis in the past ten years, three have been the greatest. The first was the world war. War demanded the closest diagnosis and taught that the unfit should not be made to serve, nor the fit allowed to escape service; that the unfit after the war should be properly cared for and the fit not allowed to remain a burden on the country. The second teacher was pestilence, influenza, and its lessons are as yet by no means all learned. Concerning the interrelation between influenza and tuberculosis in etiology and in differential diagnosis, the last word has certainly not yet been spoken. The third chief teacher has been the roentgen ray, which not only aids in diagnosis but also in illuminating pathology. The employment of surgical and nonsurgical methods of treatment represents a great advance. Artificial pneumothorax was thought out a century ago, and used a third of a century ago; yet it came into general use, in America at least, only within the past ten years. In 10 per cent of cases to which it is applicable, it increases the chance of improvement by possibly 50 per cent. Ten years ago Paterson's autoinoculation ideas had some vogue, though few followed him far in his cure by work. The two sides of the shield, rest and exercise, are alternately exhibited. Just now rest seems to be in the ascendancy, and we have rest squads, where ten years ago we had work gangs. While we all see the need of both rest and exercise, the opinion is stronger than ever that the essence of the cure to be applied early and long is rest. Food ideas have not changed much, but we have got a little further away from the fad of overfeeding and the raw egg, which was always disliked, and is now abandoned on scientific grounds. What the next ten years may bring forth no prophet can say, but means may be found for making an earlier diagnosis.—*Retrospect and Prospect: Tuberculosis Ten Years Ago, To-day and To-morrow, David A. Stewart, pamphlet, 1920.*

Some Questions Relating to Tuberculosis.—Although to some practitioners the subject of tuberculosis does not arouse enthusiastic interest, the problems are serious and many feel that there is yet much to be learned; and since it is contended that some pulmonary lesions present signs and symptoms practically identical with those resulting from the invasion of the bacillus of tuberculosis, the articles prepared by Dr. Hawes are stimulating and to some will be found to be encouraging. The first paper on this subject appears in this issue of the Journal. In connection with this subject, the recent veterinarian conference in Boston was notable because the etiological relations of bovine to the human disease are given prominent consideration. It is evident that veterinary medicine is alive to the importance of controlling bovine tuberculosis as it enters into the human problem, as well as its relation to economics. Dr. E. C. Schroeder, of the United States Bureau of Animal Industry, contended that *bovine tuberculosis can be eradicated* by a broad public policy of the general application of the tuberculin test and destruction of diseased animals. Already bovine tuberculosis has been reduced 20 per cent. in the past five years, and many pure bred herds are entirely free. Dr. John F. Devine, of Goshen, N. H., stated that "we can never eradicate human tuberculosis while we nourish it with the bovine." Breeders with the largest interests are endorsing radical measures, but the difficulty lies in dealing with small herds, for the loss of cattle is a severe tax on the man of limited means. In order to meet this objection the government must provide for an adequate indemnity. Considerable notice has been taken by the press of the views of Dr. Maurice Fishberg, expressed during the meetings of National Tuberculous Association, relating to marriage by those afflicted with the chronic form of tuberculosis. It is generally believed that such patients should not be given any general instructions in regard to important details of life or treatment, especially in daily papers, but rather have every feature of a case passed upon by a physician who is competent to decide such questions. The general publication of opinions of this sort may do great harm and lead to mental distress, for it is perfectly well known that although a pregnant woman may appear to be doing well, after parturition the disease sometimes develops very much more rapidly. If the statement had been published in a more conservative way, with instructions to always submit the question to a capable physician, less harm would have resulted. It has become the fashion to publish as much medical matter in the daily press as the editors feel may be of interest and can be made spectacular. It would be of advantage if such matter could be supervised by one with a judicial mind trained in medicine. Another matter reported among the subjects discussed by the American Institute of Homoeopathy relating to tuberculosis may also be referred to in this connection. It was stated that alfalfa and clover had been found to be of value in treating the disease. Two generations ago clover was in use among the laity as a cure for cancer, and while we all hope that more effective methods of treatment will be discovered, history should lead to careful investigation and rigid scrutiny of any drug treatment before it is made public. The people have suffered so many disappointments that we should feel that premature proclamations should not be made. The recent article by Dr. Hawes on the treatment, since given publicity in England, is very pertinent.—*Editorial, Boston M. & S. J., July 7, 1921, clxxxv, 35.*

Cure or Preventive of Tuberculosis.—The characteristics of the human, bovine and avian types of tuberculosis are described and discussed. The author concludes from his recent discussions with many of the English and French leaders, and from the recent English and French literature, that there is a spreading conviction that not much further progress will be made until a specific treatment is obtained for its cure or prevention, or both; that in all probability, this specific when found will be some living relation or modification of the tubercle bacillus; that the reason this specific has not been found before is that the tubercle bacillus has not been understood and is not understood; and that it behooves all the capable and ambitious who are engaged in tuberculosis work to study the tubercle bacillus, and to keep themselves informed of the studies of the tubercle bacillus made by their fellow workers in this and other lands.—*What About a Cure or Preventive of Tuberculosis? S. J. Maher, Med. Rec., May 7, 1921, xcix, 769.*

Pulmonary Tuberculosis Mortality Since 1914—The course of mortality from pulmonary tuberculosis during and since the world war exhibits variations of unusual interest. The data for 1919 and 1920 have not been completely tabulated but a table has been compiled giving the mortality rates per 100,000 living persons for the United States, England and Wales, the Dublin registration area, and Spain, by years, since 1914. From a study of this table is seen a definite rise in mortality, widespread and lasting through 1918, followed by a marked decline in 1919 and 1920. The high rate for 1918 was apparently due to the two waves of epidemic influenza. Presumably, many tuberculous persons were carried off by the influenza epidemic and a part of the low tuberculosis rate in 1919 and 1920 reasonably may be ascribed to the earlier removal of persons who would have died in these two years. Roughly discounting, however, the effect of the influenza epidemic, the existence of an unusual wave of mortality from pulmonary tuberculosis is still clearly shown, beginning in 1916, reaching its crest in 1917, and declining in 1918, 1919, and 1920. If there be an association between the economic conditions and the tuberculosis death rate, a possible explanation is suggested in the fact that immediately preceding the rise in mortality during 1914 and 1915 in the United States, there was a period of serious unemployment, and that in 1917–1920 wages kept pace with living costs and the demand for labor was extraordinarily great. Stevenson, in the 1919 Report of the Registrar-General, comments upon the course of tuberculosis mortality in England and Wales. He says it is remarkable that a fall in the


NEW YORK CITY DEATHS FROM TUBERCULOSIS
SINCE 1898


DEATH RATE FROM TUBERCULOSIS IN NEW YORK CITY
PER EACH 100,000 INHABITANTS, SINCE 1898

G. I. DROLET, *Statistician*
NEW YORK TUBERCULOSIS ASSOCIATION

mortality from tuberculosis occurred in 1919, notwithstanding the effects of the influenza epidemic which continued into the early part of the year. If the influenza increased the death rate by killing off tuberculous patients who would otherwise have died a little later, the great fall which has occurred since the end of the epidemic may be in part attributable to this earlier removal of tuberculous persons. There is no evidence that mortality from the nonpulmonary forms of the disease was increased by the epidemic. These nonpulmonary rates were very low in 1919, and this is thought to point to a real decline in the destructiveness of tuberculosis.—*The Course of Pulmonary Tuberculosis Mortality since 1914, Pub. Health Rep., May 27, 1921, xxxvi, 1178.*

Pulmonary Tuberculosis Mortality of Large U. S. Cities.—Denver heads the list, with a death rate of 281 per 100,000; Los Angeles next, with a rate of 154. It is not surprising that these two cities should head the list, as regards mortality from this cause, by reason of the well known fact that thousands of persons take up their abode in these cities, famous for the more or less ideal climatic conditions favorable to the cure or the arrest of this disease. Portland, Oregon, showed an extremely low rate of 54 per 100,000—that is, $\frac{1}{5}$ of the mortality as found in Denver. Rochester had the extremely low rate of 64, closely followed by Milwaukee, with a rate of 70, and St. Paul, with a rate of 71. The 3 largest cities of the country, Chicago, New York and Philadelphia, showed rates of 83, 109, and 121, respectively. The rate for the city of Boston was the same as that for New York City.—*Mortality of the Large Cities of the United States for 1920, Weekly Bull. Dpt. of Health, N. Y. City, July 9, 1921, x, 217.*

Tuberculosis in a Parish.—As the problem of tuberculosis in rural districts is obviously different from that in industrial areas, a small country parish in the county of Carmarthen was chosen for intensive investigation for the following reasons: the parish is purely agricultural; it is situated at a high altitude, but differs in no respect from other parishes; there is no manufacturing town within twenty miles; and there are no industrial conditions, generally considered favorable to the onset or spread of tuberculosis. The general conclusions may be summarized as follows: 1. Just as the rural counties of Wales suffer from a higher mortality than industrial counties, this was also the case in the county of Carmarthen. 2. The inhabitants of the parish are insufficiently and unsuitably fed. The standard of diet is universally low among laborers and farmers alike. Alcoholism is infrequent. Infants are rarely breast-fed, condensed milk being largely used. 3. Domestic insanitation is rife and common to both tuberculous and nontuberculous population. 4. The intermarriage of tuberculous stocks is lamentably frequent, and has a marked effect in maintaining the present high death rate. 5. Structural deficiency in housing does not influence the heavy death rate as much as in urban districts. 6. The unhygienic mode of life found in this parish is partly a result of poverty, but to a greater extent to bad tradition, and therefore renders the tuberculosis problem all the more difficult to solve. 7. Resistance to infection with tuberculosis is remarkably low. Institutional treatment is rarely accepted and its results are disappointing. During the period 1875–1914, approximately one sixth of the total deaths were due to tuberculosis, 81 per cent. of the deaths from tuberculosis being due to the pulmonary form.—*Tuberculosis in a Welsh County Parish, R. C. Hutchinson, Tubercle, May, 1921, ii, 345.*

Tuberculous Disease In Life Insurance Selection.—Since tuberculous infection has taken place in over 90 per cent of the human race before the age of fifty it cannot enter into the calculation of life insurance risk. On the other hand, tuberlous disease represents one of the most serious problems with which the companies have to deal. The close association of tuberculous disease wtih other lung lesions and the marked effect of other diseases upon the development of tuberculosis present additional risks. A history of pleurisy, prior to the onset of pulmonary tuberculosis, is present in from 20 to 25 per cent of the cases. Inflammation of the pleura seems to be an expression on the part of nature to limit the progress of tuberculous infection. On account of the recent high incidence of influenza pneumonia, a great many chronic lung changes will be encountered in the next few years. These will unquestionably have an unfavorable influence upon mortality. Abnormal physical signs at one apex in these cases should be considered as due to pulmonary tuberculosis until proved otherwise. At no period in the last ten years, has the author had under observation so many unfavorable cases suffering from tuberculous disease as now. More than 50 per cent of these give a history of severe influenza or influenza pneumonia. Bronchitis may also mask an underlying tuberculous lesion.

Applicants with a history of bronchitis, or where it appears in the family history, should be kept under observation before acceptance, if accepted at all. Asthma is frequently associated with pulmonary tuberculosis. Soca found it in 500 out of 700 cases, and Pottenger in 7 out of 75 tuberculous patients in his sanatorium. The author collected 36 cases of asthma in which tubercle bacilli were found in the sputum. Trousseau considers asthma and tuberculosis as an expression of the same diathesis. The combination is not so very rare. Obesity makes the prognosis worse and the lung disease usually runs a rapid course. In one private institution, 79 per cent of the patients were under standard weight for height and age and all the cases had at some time given a positive sputum. In a public institution, 62 per cent of the cases showed positive sputum and 88 per cent were under standard weight for height and age. A recent report from the Trudeau Sanatorium shows the relation existing between age and tuberculous disease in a group of 989 cases and, in addition, the present condition of patients who had passed through the sanatorium. The great campaign carried on in the United States during the past twenty years against tuberculosis has had an appreciable effect upon mortality. The degree of vital resistance of the patient is of great importance in the prognosis. A good family history is not as valuable a factor in selection as a bad family history is hazardous to selection. Partial immunity of six-sevenths of the human family must be largely the result of repeated insignificant infections. As Löwenstein has said, "Only the tuberculous are tuberculosis-immune." Immunity may also be produced by the use of tuberculin over a long period of time.—*Tuberculous Disease in Life Insurance Selection, W. B. Metcalf, Med. Insur. & Health Conserv., April, 1921, xxx, 251.*

Tuberculosis Control.—The Framingham Community Health and Tuberculosis Demonstration has made every effort to find tuberculosis, to treat the disease, to educate against its spread, and to cure known cases. All this work has been carried out with the generous aid of the local Framingham agencies, official and private. During a period of nearly four years the Demonstration has had under observation or treatment a total of 366 cases, including arrested as well as active cases. From a study of these cases the following tentative standards have been set up, any of which further experience may modify: 1. The minimum number of cases in the average community that will probably escape detection in an early stage of the disease, in spite of reasonably adequate machinery. About 50 per cent of advanced cases are undiscovered in most communities at the present time. It would seem that the application of fairly complete disease detecting devices might be expected to reduce this percentage to 4 per cent, if not to a lower figure. 2. The minimum number to die in a representative group of tuberculous individuals. In Framingham 21 per cent have died. A study of these deaths shows that 5 per cent might have been saved if the treatment machinery in the community had at all times during the Demonstration been operating with complete success. 3. The maximum number that may be reported before death. Ninety-three per cent of tuberculosis cases were reported before death, other communities reporting from 60 to 80 per cent. 4. The extent of tuberculosis in the population. A thorough examination of thousands of the population reveals active tuberculosis in about 1 per cent and arrested disease in about another 1 per cent. The average normal American community is at the present time aware of three to five known active cases for each annual death. The Demonstration during its first year, increased this ratio to 9 to 1. 5. The minimum number of cases needing sanatorium treatment. Nearly one third of the active cases in the community require institutional care and can be materially benefited. 6. The minimum number of beds required for tuberculosis treatment. A city of 100,000 people would need at least 100 institutional beds for the treatment of pulmonary and nonpulmonary tuberculosis. 7. Minimum mortality rates. Fewer cases, particularly fewer advanced ones, are found. The rate for the complete Demonstration period, 1917–1920, when compared with the previous decade, 1907–1916, represents a reduction of 31 per cent or about one third. The rate for 1920 represents a reduction of 47 per cent, or about one-half. The Appraisal Committee, which studied the Framingham work about one and a half years ago, stated that for a period of five years a rate which averaged below 90 per 100,000 would be significant, as reflecting directly the special efforts to decrease tuberculosis. If the rate for Framingham for 1921 proves to be as low as that for 1920, the average rate for the five years of the Demonstration will then be approximately 80 per 100,000, which is ten points below the average set by the Appraisal Committee. Such a rate, while gratifying, ought to be further lowered.—*Certain Minimums and Maximums in Tuberculosis Control, D. B. Armstrong, Am. J. Hyg., May, 1921, i, 278.*

Dispensary Control of Tuberculosis.—The total number of patients, tuberculous and nontuberculous, under the care of the Associated Clinics of Greater New York, was 40, 885 in 1920, as against 43,108 in 1919. Of these 40,885, there were 12,218 tuberculous patients, the remainder being either suspects or doubtful cases, and nontuberculous contacts, mostly children, kept under observation because living in homes where there was or had been recently a tuberculous member. In all boroughs, 19,103 new people came for a first examination in 1920 as compared with 20,612 in 1919. The number of readmissions of former patients was 11,150 for 1920 as against 11,096 in 1919. The total attendance during 1920 at the 29 tuberculosis clinics, now comprising the Association and covering the entire city, was 113,874, whereas it was 128,283 in 1919. The number of nurse's visits to the homes of the patients, and elsewhere on their behalf for various social services, was 61,260 in 1920 as compared with 56,853 in 1919. Preventive work for the protection of children exposed to tuberculosis has continued to be emphasized by the clinics. In 1920, 18,135 such children have been kept under observation, as against 17,770 in 1919. The proportion of children under sixteen years of age at the clinics to the total number treated has been an increasing one. The children's visits to the clinics, on the other hand, decreased in 1920, namely 43,305, as against 48,259 in 1919. During 1920, 30,940 cases were discontinued. Of these, 19,054—according to the medical records—were found nontuberculous; 8,581 tuberculous; and in the case of 3,305, no diagnosis was arrived at before the patients left the clinics. Of the 8,581 tuberculous patients, whose cases were terminated in 1920, 8,455 were of the pulmonary type and 127 were suffering from other forms of tuberculosis. The disease, at the time of the first examination of the 8,455 pulmonary cases, was incipient in 3,842, moderately advanced in 3,695, and far advanced in 918. Though many patients remain under the observation of the clinics for only a short time, sputum was reported positive for tubercle bacilli in 14 per cent of the first stage, in 28 per cent of the second stage, and in 51 per cent of the third stage cases. In New York City, on December 31, 1920, 27,919 cases of pulmonary tuberlosis were registered at the Department of Health and classified as follows: Attending tuberculosis clinics, 3,485; under the care of private physicians, 3,193; in hospitals, within the city, 3,394; out of town and in sanatoria, 3,035; remaining at home, 9,449; not found, 5,363. Though registration is acknowledged to be incomplete, these statistics show that on that day 21,490 cases of tuberculosis were a home problem in New York. About 15,000 new cases will be added during the coming year. At the time of the organization of the Association of Tuberculosis Clinics in 1907, the death rate for tuberculosis in New York City was 238 for every 100,000. In 1920, it was reduced to 126. If this first death rate had been prevailing last year, we would have had to register 13,483 instead of the 7,134 deaths which occurred. Improvements in living conditions are responsible for some of this gain; also the coöperation of other agencies. Reports, available only since 1909, show 251,729 new patients, tuberculous and nontuberculous, examined and treated; of these, 80,215 children kept under observation and care of the clinics; 36,118 patients directed to hospitals and sanatoria; and total clinic attendance equalling 1,469,557 visits paid to the doctors, nurses, and social workers. Visiting nurses paid 961,064 calls to the homes of patients and to other social agencies to instruct, comfort and aid their charges. Figures are inadequate even to suggest the services that have been rendered, but give an idea of what has been attempted to alleviate suffering among the victims of tuberculosis and for the protection of the community.—*Dispensary Control of Tuberculosis, 1920 Year Book, Ass. of Tuberculosis Clinics of New York.*

Building Tuberculosis Sanatoria.—In the preparation of standard plans for the several types of tuberculosis institutions, the needs of ex-service men as patients being especially considered, the following general requirements should be borne in mind: 1. location and site; 2. function for which buildings must be provided; 3. general layout; 4. medical administration; 5. general administration; 6. patients' quarters; 7. hospital building; 8. semiambulant patients' quarters in general; 9. semiambulant patients' quarters for cold belt; 10. semiambulant patients' quarters for warm belt; 11. ambulant patients' quarters for cold belt; 12. ambulant patients' quarters for warm belt; 13. dining halls, etc.; 14. other service and working buildings; 15. residences for staff and employees; 16. laboratories; 17 community building; 18 occupational and prevocational therapy. All these items are discussed in detail. In an appendix the requirements for laboratories for tuberculosis sanatoria and hospitals, as laid down by E. R. Baldwin of Saranac Lake, are described.—*Notes on Tuberculosis Sanatorium Planning, Pub. Health Reports, June 17, 1921.*

Standard Tuberculosis Sanatoria.—From data collected from every available source, the U. S. Public Health Service has prepared and published plans and specifications for a model sanatorium for tuberculosis patients, especially those from the World War. Where possible these plans will be followed in future Service hospital construction; and where conditions will not allow exact adherence they will be used so far as possible. The plans group the administration buildings in the centre around three sides of an open court. Facing from the fourth side, from across a roadway, stands the infirmary, its wards radiating away in wheel-spoke fashion. On the opposite side of the administration buildings, close up, is an auditorium and an open air theatre. A short distance beyond this wards for semiambulant patients are disposed along a concave arc; and a little further away are the wards for the ambulant patients. The officers', nurses' and attendants' quarters are severally grouped here and there on the right; and the industrial buildings (power house, etc.) are grouped on the left. Provision is made for occupational therapy and for vocational training for selected patients.—*From Health News, Bull. U. S. P. H. S., July, 1921.*

General Hospitals and Tuberculosis Patients.—The opening of wards in general hospitals for tuberculous patients, as recommended by the American Medical Association at its recent annual meeting in Boston, will, it is believed by the U. S. Public Health Service, be of enormous benefit not only to most of the two million known victims of the disease in the United States but also to thousands of others in whom the disease is incipient and easily suppressible, if promptly treated. Tuberculosis in this stage is difficult and often impossible of positive diagnosis, even by an expert, and many persons, even when told by their family doctor that their case is "suspicious" and that they should take precautionary treatment, fear the stigma of an avowed tuberculosis hospital and put off action until recovery has become long and difficult. In a general hospital the diagnosis will not be made public and the family will not be embarrassed; but at the same time all necessary precautions can be taken to avoid danger of infection to others. The resolution was prepared and recommended by the National Tuberculosis Association in 1916; its approval now by the American Medical Association shows a very marked change in medical sentiment. In support of the new policy it is argued that in many small cities two hospitals, one general and one tuberculous, can be run only at a loss, but if combined would pay operating expenses, especially as the combined hospital would draw many secret tuberculous cases. Many general hospitals could easily enlarge their facilities by fitting up wards, roofs, porches, and unused open air spaces and thus provide greatly needed space for tuberculous patients, both former Army men and civilians. The routine treatment of tuberculous patients in all general hospitals, instead of as at present in only about one-eighth of those in the country, should enable people in moderate circumstances to obtain preliminary treatment in their home towns instead of being forced to go without or to go to resorts. Such preliminary treatment would habituate the patient to the regimen essential to his cure and to the protection of others, and would enable him to go back to his home and get well under home treatment, as he probably would not have done without such training. Visits to the hospital will also familiarize members of the patient's family with sanitary precautions such as the sputum cup, which commonly horrifies them and is soon given up by home patients. Visits by the family physician to his patient in the hospital would familiarize him with the treatment and enable him to diagnose other cases much earlier. It would also enable him to supervise the later home treatment of both this patient and of others. At present, although tuberculosis is the most common of all serious diseases, its treatment is neglected because general practitioners are in the habit of sending their patients away. In short the result of opening the general hospitals to tuberculous patients will, it is believed, be very largely preventive, and will thus be in line with the medical tendency of the day, which is looking more and more to prevention instead of cure.—*From Health News, Bull. U. S. P. H. S., July, 1921.*

Sanatorium Treatment under County Councils.—On May first the duty of providing institutional treatment for persons suffering from tuberculosis falls to the county councils. There are divergent views as to what constitutes sanatorium treatment, both from the point of view of time and method of procedure. A tour of inspection made by experts would ultimately do much to raise the standard of sanatorium treatment. At present there is conflicting eivdence. E. Ward thinks that the calculation that 2 out of 10 early cases are cured or materially relieved by this treatment is too optimistic, while Saugman has shown that complete and permanent recovery can be effected in 8 to 9 out of every 10 early cases.—*Sanatorium Treatment under the County Councils, Editorial, Lancet, April 16, 1921 cc, 813.*

Tuberculosis Recreation Centres.—The majority of tuberculosis cases, discharged from sanatoria, though improved, are liable to a breakdown under ordinary conditions, unless something further is done for them. For this reason Collins, the tuberculosis officer of the County Borough of West Ham, England, suggests that tuberculosis recreation centres be established in populous districts. The site for such centres should be an open space easily accessible from all quarters of the district. The buildings can be of the simplest construction like wooden huts, but should be well heated, ventilated and lighted. The rooms should be comfortably furnished and supplied with periodicals, daily papers and indoor games. The plan should include a dining hut, where meals could be obtained without charge. The centre should be under medical supervision; rest and exercise of the patients suitably regulated; and plans for their daily life roughly mapped out. It might form the nucleus of a much larger scheme which might be called a tuberculosis day colony. The expansion could be accomplished by adding workshops for occupational training and granting allotments for farming produce, raising chickens, etc. The recreation centre should not in any way supplant the sanatorium for early cases nor the hospital for advanced cases. For patients whose home environment is especially bad, sleeping quarters might be provided, but the majority could sleep at home and would be better contented by such an arrangement. The centre would be used chiefly by men of the industrial class, but could also accommodate women. For married women with children some other plan must be devised that does not involve long absence from home. All children suffering from tuberculosis should be treated in an open air school or some other desirable institution. Such a plan would relieve the distress of many tuberculous people and provide, at a comparatively moderate expense, rest and recreation, food, fresh air, medical supervision, and limited segregation.—*A Scheme for Dealing with Ambulant Cases of Pulmonary Tuberculosis, F. G. Collins, Tubercle, April, 1921, ii, 306.*

The Public Health Nurse in the Campaign.—It is estimated that there are 20,000 consumptives in Massachusetts at the present time. J. S. Hitchcock has said that 80 per cent of the tuberculosis work properly belongs to the nurse, and this estimate is probably not too high. Every public health nurse should understand the essentials of successful treatment. The rest method is easy to learn and easy to teach and can be carried out satisfactorily in the home. It is not sufficiently appreciated what can be accomplished by prolonged bed rest in the open air. Correspondence classes should be formed by the State Department of Health. The patient should agree to follow strictly the detailed instructions given by the nurse and by correspondence. Reports should be made in writing to the doctor of the class at stated intervals. This plan would permit of the instruction of a large number of patients at a minimum of expense. It would lighten the work of the nurse.—*The Importance of the Public Health Nurse in the Tuberculosis Campaign, J. H. Pratt, Boston M. & S. J., May 26, 1921, clxxxiv, 537.*

Haverhill Tuberculosis Association.—Communities which are showing interest in health problems are urged to observe the work done by the Haverhill Tuberculosis Association, for this organization is one of the most progressive in the state. The results obtained in that city are due in a great degree to medical direction and oversight, acting in close coöperation with the city board of health. The people of Haverhill have endorsed the work in a liberal way. The hospital for tuberculosis patients is a model of its kind and the situation is ideal. The Association has felt that one great difficulty in the early recognition of tuberculosis has been lack of painstaking care in the early study of doubtful cases, and in order to assist physicians has prepared a simple history card for the physician's use on which may be recorded all essential facts relating to a suspected or recognized case. The value of such a card lies in keeping before the doctor suggestions of the details of the essential investigation and a record of conditions found. These cards may be obtained at the *Journal* office and at the medical supply stores at a cost of five cents each. All profits from the sale will be used to continue and extend the work in Haverhill.—*Editorial, Boston M. & S. J., June 30, 1921, clxxxiv, 711.*

Lower Lobe Tuberculosis.—Among 1000 consecutive admissions to the sanatorium at Bedford Hills, N. Y., only 3 cases of definite lower lobe tuberculosis were found. Lower lobe lesions occurred in 18 other cases; but after careful study, 17 proved to be nontuberculous, and in 2 patients old tuberculous lesions were found at both apices, in spite of the fact that extensive physical signs existed at one base and that the upper lobes appeared to be normal. Of the 17 nontuberculous patients, 11 suffered from chronic nonspecific inflammatory conditions, and 5 from bronchiectasis.—*Chronic Pulmonary Tuberculosis Primarily in the Lower Lobe, J. Rosenblatt, J. Am. M. Ass., June 11, 1921, lxxvi, 1647.*

Pathology of the Mediastinal Lymph Nodes in Tuberculosis.—Gloyne examined in detail the mediastinal nodes in 5 tuberculous and 3 nontuberculous cases by dissecting away every bit of lung tissue, slicing through each node, and counting the total number of nodes in each group. The total number of nodes draining the lung, that is, superior and middle mediastinal, varied from 36 to 79 in the tuberculous and from 40 to 65 in the nontuberculous cases. On the average there were 9 tracheal, 35 interbronchial, 5 bifurcation, and 10 superior mediastinal nodes (right and left sides added together). Only 4 calcareous nodes were found in the tuberculous cases: 2 in the bifurcation, 1 in the right tracheal, and 1 in the left interbronchial group. Two of these had been noted in radiograms during life. No calcareous nodes were found in the nontuberculous cases. Apart from calcification, naked eye evidence of disease was not marked in the nodes from tuberculous cases, except in one case where every node showed small caseating tubercles. A fresh series examined microscopically, however, showed typical tubercles with giant cells in 12 out of 18 nodes, and tubercle bacilli in all. There was not sufficient variation in the microscopic lesions in the different groups of nodes to demonstrate the line of march of the tuberculous infection along the mediastinal chain. Anthracosis was noted in the nodes of all the cases examined, except in that of a child of four. The interbronchial group was most densely pigmented, showing signs of anthracosis even in the four year old child. Theoretically, soot should produce no shadow in a radiogram. In experiments on rabbits inoculated with suspensions of coal dust, no shadow was produced, except if placed in a sufficiently thick layer. It seems possible, therefore, that carbonaceous particles, such as soot, coal dust, etc., may cause an increase in the thickness of the gland which would give a sufficiently dense shadow to cause confusion with lymph node enlargement due to microscopic tubercles. Calcareous nodes are readily distinguishable in the radiogram because of the extreme density and sharp outline of their shadows. The shadows produced by anthracosis, caseation, microscopic tubercles and malignant disease did not afford sufficient differentiation to warrant definite conclusions.—*A Note on the Pathology of the Mediastinal Glands in Tuberculosis, S. R. Gloyne, Tubercle, April, 1921, ii, 300.*

The Diagnosis of Tuberculosis.—Academically it is possible that 50 per cent of the world's population is suffering from tuberculosis. The practical test is the finding of the bacillus in the sputum or lesion. This test is positive in 70 per cent of severe cases, but only in 30 per cent of all cases. Samuel Gee taught that a pulmonary lesion which does not clear up in six weeks is either tuberculosis or empyema. Two exceptions to this would be pneumokoniosis or the dust phthisis of miners and stone cutters, and chronic bronchial catarrh, as it occurs in the poorer districts of big cities like London and Manchester. The author disagrees with the general opinion as expressed by Gee, in that he believes miners' phthisis is always tuberculosis engrafted on an irritated lung and that chronic bronchitis is also tuberculosis and will respond satisfactorily to treatment by insufflation in from two to three weeks.—*Diagnosis in Tuberculosis, O. Paget, Med. Rec., June, 11 1921, xcix, 1005.*

Gassing vs. Tuberculosis.—Our public health hospitals, sanatoria, and convalescent homes are filled with men suffering, as they believe, from tuberculosis, but in reality from the late effects of gas poisoning. Many of these patients have been diagnosed as tuberculous because of certain symptoms common in tuberculosis, and because many physicians have not learned to make a differential diagnosis between tuberculosis, gas poisoning, influenza, trench or barrack-room bronchitis, and nervous exhaustion. Of the immediate effects of gas much is known; of the late effects, very little. Gases owe their efficiency to their irritative and escharotic effects on the respiratory tract, and the contraction of the scars thus produced may, and often does, lead to serious and progressive mechanical difficulties, not only to the ingress and egress of air into the bronchi, bronchioli and alveoli, but to the pulmonary circulation as well. It is also known that these gases have a certain selective action. Mustard gas affects chiefly the upper air passages; chlorine gas injures the lining of the entire respiratory tract, resulting, frequently, in chronic lung lesions; phosgene, least severe in its immediate effects, often leads later on to serious injury of the lung tissue. The basis of these changes caused by gas is a proliferative fibrosis which destroys, to a greater or less extent, the natural protective properties of the bronchi and leads to their invasion by secondary organisms. If tuberculosis plays a part in this secondary invasion, it is a minor one. X-ray examination of the lungs in these gas cases shows a very definite picture. There is usually considerable increase in the tissues around the hilum of the lung, marked increase of peribronchial tissues extending toward, but rarely into the parenchyma, and more toward the bases than upward. The apices themselves are usually clear. In addition to this, there are often localized areas of dense fibrosis. There are two groups of symptoms presented by these gas cases; pulmonary and the constitutional. Prominent among the first are cough, expectoration, hemorrhage, pain, or a sense of constriction in the chest, dulness, usually at the bases and due to a thickened pleura, diminished voice and breath sounds due to the same cause and râles of every variety and description. Among the constitutional symptoms are loss of strength, fatigue, shortness of breath, signs and symptoms of a marked psychoneurosis and increased reflexes. Fever, rapid pulse, loss of weight, anemia and other symptoms characteristic of tuberculosis, are conspicuous by their absence. The majority of these men go under the diagnosis of pulmonary tuberculosis. They often give a history of sudden, acute febrile attacks with or without cough and sputum. These attacks disappear as suddenly as they come, leaving a feeling of intense lassitude, which lasts for a considerable time. Such sudden attacks are characteristic of these late gas cases. These men require rest away from a medical atmosphere, and, particularly, sympathy and encouragement. An outdoor life should be prescribed. The man who has been gassed should be treated; not his lungs.—*Diagnostic Pitfalls. The Late Effects of Gassing vs. Tuberculosis, John B. Hawes, 2nd, Boston M. & S. J., July 7, 1921, clxxxv, 1.*

Fatigue as a Test of the Tuberculous.—When the resisting powers are low, under the influence of fatigue the organism uses up its nitrogenous reserves and finally the albumin of its own tissues. It is possible to determine the lowering of the nitrogenous reserves by investigating the intermediate nitrogen metabolism in the blood and the changes in weight of the body. This has been worked out at Maragliano's clinic by Sivori, and has formed a reliable means of ascertaining the resisting powers in the tuberculous to aid in allowing exercise or self-support and in estimating the effect of treatment. For practical purposes it is sufficient to record the changes in weight. For this the patient is kept in bed in absolute repose for ten days, with a diet of from 2,200 to 2,300 calories, including from 90 to 100 gm. of protein. The diet is kept at a constant figure, and every day at the same hour the weight is recorded. By the sixth day if the weight remains stationary or has increased, the patient can get up and take a daily walk of 2 km., for a ten day period. If the weight diminishes, there is little hope of organic resistance. If it remains stationary or increases, the walk is increased to 4 km. for another five days. If the weight diminishes then, we can assume a slight margin of resistance. If it does not diminish during this time nor in another five day period, other conditions equal, we can say that the individual has a good margin of organic resistance, and is capable of responding to specific treatment which requires the active participation of the organism.—*La fatica come elemento di studio del margine di resistenza organica nei tubercolosi, V. Pietroforte, Rif. Med., December 18, 1920, xxxvi, 1169.*

Weight Prediction.—In a previous paper the authors traced the development of the various measurements of the length of the body, not including the legs. They reported the results of their experiments with Bornhardt's method of estimating body weight, and discussed the sitting height recently urged by Pirquet, and the stem-length formula proposed by Dreyer. Dreyer realized, as had Bornhardt but practically no one else before him, that in predicting weight in adults, age was of small use, and that even body length alone was inadequate. Like Bornhardt, he made simultaneous use of the chest measurement, but substituted stem-length for stature, and constructed his formula in an entirely different fashion. To do Dreyer justice, it is important to test his combined formula, using not only chest girth, but also stem-length. Pirquet, in connection with a new and elaborate system of feeding, based on milk values instead of on calories, proposed a new formula for determining the state of nutrition. He had observed that a measurement little noticed hitherto, the sitting height, stands in close relation to the cube root of the body weight. Trial of these new methods appeared important. Pirquet had given no original observations sufficiently complete to serve as a basis of comparison of the three methods, and Dreyer had published observations on only 16 subjects. In this paper, the authors report their observations on 16 healthy males in addition to the 16 reported by Dreyer. The ages ranged from thirteen to fifty-two years. The weights of these thirty-two healthy males were predicted by Pirquet's formula with an average error of 17 per cent, by Bornhardt's with an error of 8 per cent, and by Dreyer and Hanson's method with the low error of 4.47 per cent.—*Weight Prediction by the Formulae of Bornhardt, of Von Pirquet, and of Dreyer, H. Gray and H. F. Root, Boston M. & S. J., July 7, 1921, clxxxv, 28.*

Intrathoracic Movements.—Just as in ordinary photography, so for a good X-ray plate two requisites are essential. The object must be at rest and there must be differences in density of the various parts to be rayed. The latter condition is ideal in the chest, but there is no voluntary control over the motion of some of the organs involved. The act of inspiration raises the chest walls, causes the diaphragm to descend, and allows the inrush of air into the area of negative pressure. If inspiration is not complete, the proper density contrasts are not produced and an X-ray picture results similar to that characteristic of tuberculosis. The action of the chest wall in respiration is voluntary and usually easily controlled, as in the diaphragm, but many individuals, especially children, cannot control it. Abdominal lesions restrict its action and true adhesions, as well as nerve lesions, alter its movements. With a lung stiffened with congestion, the diaphragm may lag in its descent owing to a high negative pressure, the air not rushing into the lung to aid its movements. This may simulate adhesions and be confusing. The action of the heart is involuntary and because of its close proximity to the lung its motion may be transmitted to the lung. The great vessels, especially the aorta, have considerable movement due to pulsation which is opposite in time to the heart. The esophagus has definite movements which are revealed by an opaque meal. The lung itself moves in respiration; the fluoroscope shows that on inspiration with the general expansion of the lung the lower bronchi move downward while the upper ones move upward. The author has found that this bronchial motion may be as much as twice the width of the bronchus, but varies in different individuals and according to the violence of the heart action. In order to take correct X-ray pictures of the thoracic viscera, it must be done practically instantaneously. It is now possible to take chest pictures in less than one-tenth of a second. With this method the heart and diaphragm are sharply outlined, the individual components of the hilum differentiated, and the walls of the bronchi plainly shown. The beading of early tuberculosis, the pocketing of bronchiectasis, and early septal changes or beginning alveolar congestion can be visualized and studied. One illustration shows a radiograph made by studying the heart cycle and getting the exact interval between complete systole and diastole. The exposure was made during systole and diastole on the same film, each exposure being less than one-tenth of a second.—*A Study of Introthoracic Movements, W. W. Wasson, Colorado Med., April, 1921, xviii, 76.*

Lung Mapping with Bismuth Mixtures.—*Summary:* Bismuth mixtures can be injected into the bronchi and lung of living patients without doing harm. The injection of opaque substances into their lungs will open up an enormous field of usefulness in the study of cough, the expulsion of secretions from the lung and lung drainage. It will also localize bronchial strictures in the same manner as occurs in the esophagus. Furthermore, it will be of the greatest aid to the thoracic surgeon by mapping out the abscess cavity in that lobe of the lung on which he is to operate. A definite lung abscess cavity is seldom seen bronchoscopically. Pus is usually seen coming from a small branch bronchus, and the abscess cavity may be well around a corner and not in a direct line with the bronchus from which the pus is oozing. An injection of a bismuth mixture or some other opaque substance will clear up this error. Bismuth when it enters the abscess cavity is interpreted in the radiographic plate by its metallic lustre, and when it is in the lobular lung structure it is interpreted by its dull opacity. Pus diffuses and soaks the lung structure, and this often makes the involved area appear many times larger than it really is. The amount of bismuth injected in these patients was an 8 cc. mixture of bismuth subcarbonate in pure olive oil, 1 in 2 and 1 in 3. The mixture is sterilized by boiling. The injection should be made slowly and not with a squirt, for the picture may be spoiled by bismuth soaking the lung. From these preliminary studies it seems that cough and the action of cilia may not be the only means of expelling secretion from the lung. While bismuth mixtures were originally injected by the author for purposes of lung mapping of abscess cavities in their proper lobes, it seems to have been of apparent benefit to the two patients in whom it was tried. So far it has done no harm.—*Lung Mapping by the Injection of Bismuth Mixtures in the Living, H. L. Lynah, N. York M. J., July 20, 1921, cxiv, 82.*

Striae Distensae in Consumptives.—The occurrence of striae in pulmonary tuberculosis seems to be very rare, or, at least, little observed; at any rate, little has been published. Among 5,800 patients treated at Boserup sanatorium (Denmark) the author found 12 who according to the records exhibited striae. Four of these he observed himself. Three salient features emerge from the study of the records of the above 12 cases: (1) the great gain of weight in a short period; (2) the youth of the patients whose ages were within the narrow limits of fourteen and twenty-two years; and (3) the preponderance of males over females (10 to 2). The gain of weight was so great (from 7 to 24.7 kilos) and so constant, that it may be surely regarded as an essential factor in the causation of the striae. Their appearance in places where accumulations of fat are most prominent, that is, the hips, loins, and shoulders, further supports this view. There was nothing to suggest that they could be associated with any compensatory dilation of the healthier side of the chest, for they never occurred on the thorax itself, and their distribution could not in any way be correlated with the site of the disease. In most cases the disease had lasted only a short time, and there had been little or no fever to indicate marked toxemia. Any appreciable reduction of the vitality and nutrition of the skin by toxic influences can, therefore, be excluded. The marked gain of weight in itself suggests that the toxins of the disease cannot have affected these patients greatly.—*Striae Distensae in the Skin of Consumptives, K. Hammer, Tubercle, May, 1921, ii, 349.*

The Blood Pressure in Pulmonary Tuberculosis.—The auscultatory method has been used as the most accurate. When numerous observations are made at frequent intervals in cases of pulmonary tuberculosis, fluctuations in the blood pressure are noticed from time to time, but the general trend in advancing disease is downwards. The diastolic pressure is less affected than the systolic and its variations less reliable. When the minimum pressure reaches below 60 mm. Hg, the general tone of the patient is poor and progress towards recovery is, in consequence, retarded. An instance is given of a patient whose diastolic index ranged between 50 and 36 mm. Hg., with a systolic of 120. He suffered from a general feeling of lassitude with morning headache and muscular pains. With eleven months residence in the sanatorium his condition improved only slightly, although clinical examination revealed no extensive lesion in the lungs. However, if the systolic pressure is low, namely, 90 to 100 mm. Hg., the outlook seems to be better when the diastolic pressure shows a corresponding decline. But if it registers in such cases between 70 and 80 mm., making a pulse pressure of about 20 mm., the chances of improvement are not so promising. These patients have weak hearts. They are fragile, lack vitality and do not respond well to treatment. All these observations were made on male ambulatory patients in whom the temperature chart failed to show any unfavorable signs.—*Blood Pressure in Pulmonary Tuberculosis, A. G. M. Grant, Tubercle, May, 1921, ii, 337.*

The Intracutaneous Tuberculin Injection as Revealed by the Capillary Microscope.—A study was made in the living subject of the capillary vessels and superficial tissue at the site of an intracutaneous tuberculin test. The method followed was that proposed by Weiss, consisting of transillumination of the skin through paraffin oil or old oil of turpentine, by means of direct sunlight or strong artificial light (Leitz microscope lamp). Observations were made with the Zeiss binocular microscope, permitting a magnification of 35 diameters. During the first 6 hours after injections, alterations in the skin structure were of a mechanical nature, in no way characteristic of a tuberculin reaction. Thereafter, any reaction occurring was of a specific nature, and consisted of inflammatory changes involving the vessels, papillae and horny layer. By means of this technique, with a little experience and a control injection of physiological saline solution, the result of an intracutaneous tuberculin test may be foretold many hours before the macroscopic picture can be differentiated.—*Das kapillärmikroskopische Bild der intrakutanen Tuberkulininjektion, O. Lade, Arch. f. Kinderh., August 31, 1920, lxviii, 58.*

Chondroturia in Pulmonary Tuberculosis.-At necropsy of severe phthisis, marked fatty degeneration of the renal parenchyma is usually found. This is apt to give during life the reaction for chondrotin-sulphuric acid. This reaction is positive if marked cloudiness occurs in 5 cc. of urine, after adding a few drops of dilute acetic acid and 1 per cent horse serum. Among 175 severe cases albumen was found in 20, or 11.4 per cent, and chondrotinic acid in 85 or 42.8 per cent. Of the latter class 61 were tested 10 or more times. Twenty-four of these 61 retrogressed. In the others the general condition and the state of the reaction showed little harmony. The prognostic value is limited.

The constant presence of the reaction makes prognosis doubtful. Just as urobilinuria denotes liver damage, so does chondroturia indicate kidney damage.—*Über Chondroturie bei Lungentuberkulose, K. Dietl, Wien. klin. Wchnschr., March 24, 1921, xxxiv, 133.*

Alcohol Extracts of the Tubercle Bacillus as Antigens.—The authors consider the peptone B_2 antigen of Calmette and Massol and the egg antigen of Besredka the most active tubercle bacillus antigens, but point out that the former is obtained only by the use of a peptone rich in albumose, not always available, while the Besredka antigen keeps but a short time. Alcoholic antigens, such as that described by Petroff, have been too little sensitive in the case of ethyl alcohol, or excessively so in the case of methyl alcohol. The authors have modified the alcohol extraction method of preparation by preliminary treatment with acetone, previous investigations having apparently shown that the acetone removes a great number of lipoids inessential to the reaction, leaving the essential phosphatids. Their method is as follows: Tubercle bacilli grown six weeks on glycerol broth are sterilized at 120°C. for one-half hour, washed with water, dried in the oven, and left in contact with 100 volumes of acetone for twenty-four hours. The mass is then filtered off and treated with alcohol in the same proportion for ten to twelve days at 38°C. The mixture is filtered and the clear extract diluted 1:10 for use. Such an extract deposits a light precipitate on cooling and gives an opalescence comparable to a 1:10,000 lecithin emulsion in water. Titration of antigens prepared by this method showed that human and bovine tubercle bacilli and diphtheria bacilli were rich in antigen reacting with antituberculous serum, while avian and piscine tubercle bacilli and paratubercle bacilli had a moderate concentration, and streptococci and pneumococci were lacking in such antigen. The methyl alcohol extract equalled the antigen of Besredka in activity. It proved to be rigorously specific; exceptionally, it reacted with syphilitic sera, but in these cases tuberculosis could not be ruled out. The methyl alcohol extract is more active than the ethyl alcohol product and may be kept indefinitely in the absence of air, light and moisture.—*Recherches sur la valeur antigène des émulsions bacillaires et des extraits éthyliques et methyliques de bacilles tuberculeux, S. Nègre and A. Boquet, Ann. de l'Inst. Pasteur, May, 1921, xxxv, 300.*

Specificity of the Besredka Antigen.—The complement fixing power of Besredka's antigen was tried in the presence of 1:20 emulsions of the bacterial bodies of a variety of organisms. Antituberculous horse serum, prepared by repeated inoculation with tubercle bacilli, and serum from human tuberculous subjects, in contact with the antigen of Besredka, fixed alexin in high amount. The same sera behaved like normal sera in the presence of other antigens, including streptococcus, pneumococcus, B. coli, B. typhosus, B. paratyphosus, B. mallei, B. anthracis and B. subtilis. In 3 cases out of 20 a positive reaction was noted with the serum of tuberculous patients and a diphtheria antigen. The sera of horses immunized against various bacteria did not give positive reactions when used with the tubercle bacillus antigen, except in the case of the antiserum to B. diphtheriae, when a weak fixation occurred. The serum of typhoid fever, erysipelas and nephritis patients did not give positive complement fixation with the Besredka antigen.—*De la spécificité de l'antigène tuberculeux de Besredka, A. Urbain and B. Fried, Ann. de l'inst. Pasteur, May, 1921, xxxv, 294.*

Significance of Types of Tubercle Bacillus.—Notwithstanding the vast epidemic importance of human tuberculosis, it has no significance as a cause from which its epizoötic prevalence may arise. The occurrence of bovine tuberculosis among human beings, especially children, is wholly chargeable to the epizoötic prevalence of tuberculosis among cattle. While it is a serious evil which should be fought with unremitting energy, it does not lead to the dissemination of tubercle bacilli, and therefore has no significance as a cause which contributes to the perpetuation of tuberculous disease. The widespread, practically epizoötic prevalence of tuberculosis among hogs is chargeable to the epizoötic prevalence among cattle, but is in itself insignificant as a cause which contributes to the perpetuation of tuberculosis. The epizoötic, really panzoötic, prevalence of tuberculosis among cattle is entirely due to the bovine type of the tubercule bacillus, and tuberculosis among cattle is a great self-perpetuating plague. The bovine type of the tubercle bacillus is a pathogenic parasite which is not only seriously destructive to its specifically true host, but a parasite which, making its attack through its true host, also causes tuberculous disease, epidemic and epizoötic in character, in foreign hosts, through which it does not perpetuate itself. The epizoötic prevalence of tuberculosis among fowls is dependent upon the avian type of the tubercle bacillus, which lacks the power to serve as the cause of an epidemic or an epizoötic occurrence of tuberculosis among mammalia. The human and the bovine types of the tubercle bacillus have no significance as a cause for the epizoötic development of tuberculosis among fowls. The difference in the pathogenic ranges of the several types of the tubercle bacillus is very impressive. It seems clear in the light of our present knowledge that the human and the avian types, though they occasionally are found in other than their specifically true subjects or hosts, are each responsible for only one plague-like manifestation of tuberculous disease. But the bovine type, though its perpetuation depends almost entirely on its growth and multiplication in its specifically true host, the bovine species of animals, is the true cause of three important plagues, a human, a bovine and a porcine, and, in addition, is responsible in most instances for the less common occurrence of tuberculosis among other domestic mammals than cattle and hogs. It is the supremely pathogenic type of the tubercle bacillus.—*The Epidemic and Epizootic Significance of the Different Types of the Tubercle Bacillus, E. C. Schroeder, J. Am. Vet. M. Ass., July 1921, lix, 434.*

Culture of Tubercle Bacilli on Egg Yolk.—The medium contains nothing but egg yolk, soda and water. Three hundred and fifty cc. of egg yellow are stirred in distilled water and treated with 1 per cent soda solution until a thin bulk of it taken for test is transparent. About half the volume of the egg yolk is required usually. The mixture is then diluted to 7000 cc., or twenty times the volume of the egg yolk, placed in flasks and autoclaved at 110° C for twenty minutes. No meat extract, peptone, salt or glycerol is added. Following large inoculations of tubercle bacilli, growth is noted on the following day and proceeds rapidly. On the fourteenth day the medium is suitable for the preparation of antigen for complement fixation. The antigen consists simply of such a culture sterilized and rendered homogeneous by agitation. No matter how old, such cultures do not give the characteristic odor of tuberculin; yet they are quite rich in the latter, as can be shown by appropriate tests on tuberculous animals.—*Culture des bacilles tuberculeux dans du jaune d'oeuf, A. Besredka, Ann. de l'inst. Pasteur, May, 1921, xxxv, 291.*

Pulmonary Tuberculosis in the Aged.—Tuberculosis is not uncommon in the old, although the symptoms are very mild and inconspicuous, thus rendering the diagnosis difficult. Among 20 such patients, ranging in age from sixty-four to eighty-two years, the history disclosed little in the way of former hemoptysis or febrile attacks. At most these persons complained of weakness recurring occasionally after exposure to cold. Their general condition was relatively good. Dyspnea was frequently present, especially on exertion. Cough was almost constant and of long standing, but expectoration was often lacking, the sputum being swallowed, as in children. Bacilli were found in 8 out of 12 cases. Auscultation was sometimes attended with difficulty, because signs of emphysema almost completely masked those of tuberculous disease. Under these circumstances the complement fixation reaction for tuberculosis was used for diagnostic purposes, with marked success. Besredka's antigen was always used, and the technique was that of Bass and of Goldenberg-Fried. Seventeen of the 20 patients yielded a positive reaction; one of the negative cases had very advanced tuberculosis, with prospects of early fatal ending. The results lead the author to subscribe to Calmette's statement that a considerable proportion of the deaths ascribed to chronic bronchitis should actually be considered due to tuberculosis. Attention is called to the danger of undetected cases of tuberculosis in old persons among their family associates. Calmette has related an instance of three successive deaths from tuberculous meningitis in children cared for by an old governess with chronic bronchitis.—*La valeur de la reaction de fixation dans le diagnostic de la tuberculose pulmonaire du vieillard, G. Ichok, Paris Méd., January 15, 1921, xi, 58.*

Tuberculosis in Nurslings.—Tuberculosis is frequent in nurslings, its frequency increasing with the age of the infant. Both sexes are equally attacked during the first year of life but, during the second, males suffer much more than females, the ratio being 5 to 2. In nearly 50 per cent of the cases there is a history of tuberculosis in the parents.

Familial contagion is of the highest importance, hence illegitimate babies are less often afflicted. When a nursing mother presents open tuberculous lesions the baby runs great risk of being contaminated. Two facts dominate the history of tuberculosis in nurslings. The first is that tuberculosis of the bronchial lymph nodes is almost invariably the first important focus of bacillary infection; it is the most constant localization and is found in most cases. This leads one to suppose that the usual entrance of the bacillus in nurslings is the respiratory tract, and it is exceptional to discover lesions which would indicate an intestinal origin of the infection. The second fact is that tuberculosis in early life tends to diffusion and this tendency is all the more marked the younger the child.

The respiratory forms vary. The tracheobronchial adenopathy, which is nearly always present, may be latent and merely cause pyrexia. Or it may give rise to physical signs or compression symptoms and occasionally to laryngeal phenomena. Bronchitis with a subfebrile state is frequent during the first year of life, offering a very commonplace aspect, but the general health of the baby and tuberculosis reactions will indicate its true nature. The infant may recover, but if he dies autopsy will reveal an ordinary bronchitis kept up by adenopathy; or an ulcerating pulmonary tuberculosis, unsuspected during life, may be found. Bronchopneumonia, frequent during the second year of life, has a bad prognosis. Sometimes localized in foci, at other times diffuse, it is usually characterized by the persistence of its symptoms and the profound changes in the general health. At autopsy, the usual lesions of bronchopneumonia, with or without distinct lesions of tuberculosis, will be found. Ulcerating pulmonary tuberculosis is difficult to diagnose in nurslings; even cavities often remain latent; but when hemoptysis occurs, which is very uncommon, it is a sure symptom of this process. Pleural manifestations are rare and consist of a purulent collection due to the ordinary forms of infection. The dry forms are found only at necropsy.

The digestive manifestations may be divided into simple dyspepsia and gastroenteritis. The former is observed especially during the first year of life and is characterized by emaciation and hyperthermia which are disproportionate to the intensity of the digestive symptoms, the latter being in reality mild. Death often occurs in one to three months. Gastroenteritis, which is quite as frequent during the second as during the first year of life, offers the ordinary clinical aspect of this affection, but its characteristic is that no improvement occurs in spite of a perfectly regulated diet. The nature of these processes is often obscure, and as they cannot be attributed to tuberculous changes in the digestive tract, it is probable that their causal factor resides in tuberculous intoxication.

External tuberculous manifestations are not very uncommon in nurslings, particularly osteitis, Pott's disease, spina ventosa, orchitis, subcutaneous gummata and, more rarely, tuberculides.

The most frequent nervous manifestation of tuberculosis in nurslings is meningitis, while its forms are rather remote from the classified type met with in older children. The eclamptic and somnolent forms are common, likewise the form with paralytic localizations.

Generalized tuberculosis in nurslings often assumes the form of chronic miliary tuberculosis with tubercles scattered throughout the thoracic and abdominal viscera. Clinically, it is made evident by atrophic cachexia with apyrexia, polyadenopathy, and enlarged spleen and liver. Generalized tuberculosis may assume an acute course, either the asphyxiating or the typhoid forms.

In all these various tuberculous processes in nurslings, autopsy usually reveals far more extensive and advanced lesions than were suspected during life, and reactions toward healing are rarely found. Like all chronic infectious processes tuberculosis may act on the bone marrow and cartilages of ossification, thus producing rickets, and the latter condition during the second year of life has been shown by Marfan and Mantoux to depend frequently upon tuberculosis. The diagnosis of tuberculosis in nurslings depends essentially upon tuberculin reaction, and the cutireaction should be the clinician's guide. A positive result will often clear up the nature of symptoms of what was thought to be an ordinary affection, of the first two years of life.—*Editorial, Med. Rec. July 9, 1921, c, 69.*

Study and Treatment of the Pretuberculous State in Infancy.—In order to recognize the signs suggestive of predisposition to tuberculosis, the ensemble of physical attributes of the pretuberculous must be studied. Though infantile tuberculosis is almost always acquired rather than inherited, the physical condition of children of tuberculous parents is such that they are exceedingly susceptible to the disease. Proper and persistent therapy is always effective, even if an infant is already harboring bacilli in a latent focus which needs only some intercurrent infection to start their multiplication. The history may show impaired development, or unusual susceptibility to gastrointestinal or respiratory disturbances. Important signs to be noted on inspection are pallor, transparent skin, long, slender neck, narrow chest, prominent scapulae, blue network of superficial veins, child undersized for its age with long legs and large knees, slow movements, fatigue of obscure origin and susceptibility to chilling. The skin is often the site of chronic or recurrent lesions, ichthyosis being among the most important. The following signs are of diagnostic value, especially if some of them are combined: dolichocephaly, blepharitis, discharging ears, hypertrophy of the bronchi, bronchiectasis, scoliosis, one or all forms of thoracic deformities and any degree of malnutrition. Parents must be warned that the possibility of a cure depends entirely upon the care with which they will follow instructions. Spoiled children are more likely than others to be sick; they are less likely to be cured. Exercise, work, play, study, sleep and bathing should all be given in correct amount for the individual case. The value of fresh-air baths and of exposure is [illegible] known. Clothing should be light, and should be so arranged as to interfere with the movements of the child. Overfeeding is one of the greatest errors that can be made. A regular [illegible] feeding of wholesome food must be carried out. Concerning the best climate for predisposed children, high altitudes, with few fogs in winter, mixed [illegible] and [illegible]. [illegible] cases, however, and cases with [illegible], would do better at low altitudes, because of the [illegible] of the winter months. They should not be sent to resorts frequented by patients with manifest tuberculosis. The seashore is not preferable to the [illegible]. Sun baths should be given, and those with [illegible] should all be [illegible] without a [illegible]. The [illegible] are often [illegible] in [illegible], and as far as possible such [illegible] should be made up. Combined [illegible] and [illegible] therapy was found to give good results in selected cases.—*Prevention of Tuberculosis in the Predisposed Child*, P. [illegible], *Jour. de Méd. de Lyon*, April, 1921, [illegible].

Congenital Pneumothorax in an Infant.—This condition is extremely uncommon. The patient, a boy of eighteen months, was admitted with dyspnoea, cough and cyanosis. He had measles three months before admission and since then lack of appetite, constipation, wasting and night sweats. On examination the child appeared extremely ill. There was diminished respiratory movement over the left side of the chest with hyperresonance and diminished breath sounds. Over the right chest there were pronounced resonance, bronchovesicular breathing and fine râles. The heart was displaced to the right. The liver and spleen were palpable. Complicated pneumothorax was diagnosed. The child died within twelve hours. Postmortem examination revealed the left lung to be collapsed upon its root, a solid mass of tubercles, with a cavity in the apex; the left pleura studded with tubercles. The right lung contained many miliary tubercles. The hilum nodes were slightly enlarged and hyperaemic but not caseous; the liver and spleen were studded with tubercles. The mesenteric lymph nodes were much enlarged. The infection probably travelled from the mesenteric to the mediastinal lymph nodes and so along the trunk, set up areas of caseation up to the left pleural surface which later became adherent to the surrounding parts. Some [illegible] of coughing the portion of diseased tissue between a bronchus and the left pleural cavity gave way, probably three weeks before death, judging from the history. From the sudden massive infection of the pleura, general miliary tuberculosis resulted.—*A Case of Congenital Pneumothorax in an Infant, Due to Pulmonary Tuberculosis*, C. [illegible], *Brit. M. J.*, April 9, 1921, no. 3145, 532.

Epituberculous Infiltration of the Lungs in Tuberculous Infants and Children.—The authors describe a form of pulmonary infiltration to which they have given the name epituberculosis, occurring only in tuberculous children but presenting characteristics which entitle it to special consideration and classification. It was seen only in children during the first three years of life, the youngest being seven months. Briefly, the picture was as follows: a history of severe [illegible] cough with anorexia, pallor, loss of weight and occasional slight fever. Examination of the lungs revealed, usually over the upper lobe, a large area of dulness and bronchial breathing, with comparatively few râles and no signs of cavity or pleuritic exudate. The spleen was often enlarged, but heart and vessels were normal. The leucocyte count was normal, the Pirquet reaction was strongly positive, and many children had other evidences of tuberculosis, such as bone lesions, cervical adenitis and tuberculous [illegible]. The roentgenogram showed a dense, rather homogeneous shadow extending from hilum to periphery. Is this pulmonary infiltration due to specific tuberculous lung changes, or to a chronic nonspecific infiltration in the presence of a [illegible] tuberculous infection? The latter view seems to be the correct one. Children with such lesions usually recover after a long time, and the roentgenogram shows a gradually receding shadow, from periphery to hilum. The ultimate picture shows a clear lung, with no evidence of any tuberculous changes.—*Die epituberkulöse Infiltration der Lunge bei tuberkulösen Säuglingen und Kindern*, Helene Eliasberg and W. Neuland, *Jahrb. f. Kinderh.*, 1920, xcii, 3rd ser., [illegible].

The Physical Development of Tuberculous Children. Two groups of children form the basis of this study. The first (control) group of 614 children, of nontuberculous parentage, either had no symptoms, or, if they had, were negative to tuberculin tests. The second group of 508 patients were children of tuberculous parentage, or were suspected of tuberculosis because of poor physical condition, or were referred to the tuberculosis department from the pediatrics dispensary after a positive diagnosis had been made. No case was regarded as positive unless it gave the characteristic reaction to tuberculin. Tuberculosis in early childhood remains an acute disease over an undetermined number of years, and there is no method which enables one to determine the activity or quiescence of the infection. Given a group of children below the norm in height and weight, the tuberculous child will more frequently appear to be of normal height but far less often of normal weight. The tuberculous individual is often seen as the lanky child. *Conclusions:* 1. Using height and weight as the basis of comparison, tuberculous children more frequently attained the normal standard of gain that did those of the control series. 2. Neither the entire tuberculous nor control series reached the Children's Bureau standard, represented as 100 per cent, although the tuberculous group more frequently approached it. 3. The superiority of the tuberculous over the control series in gain, depend on the improvement in sanitation and food, and the removal of defects. 4. The child with hilum or tracheobronchial node tuberculosis in a group of underheight and underweight children, when properly treated, will more often be the one to attain the normal gain. This observation is equally applicable to cases seen in private practice.—*The Physical Development of Tuberculous Children, M. L. Blatt, Am. J. Dis. Child., June, 1921, xxi, 575.*

The Grancher Institute. Grancher believed tuberculosis is not hereditary, but contagious in origin. The Institute he founded seventeen years ago for the protection of children from tuberculosis proves the soundness of his theory. When tuberculosis attacks a family living in confined quarters and strikes down one of the parents, infection of the children is nearly always inevitable. The Institute takes the healthy children from the tuberculous family and places them in the country, in the families of healthy country people, where they pass their school life up to or beyond the age of thirteen. Excellent country doctors choose the homes of the foster parents and look after the children without charge. The predisposing indirect causes of tuberculosis, as well as the immediate cause, the contagion in family life, are thus eliminated. The child put in a good home with fresh air and abundant, nourishing food, becomes a new being, physically and morally, and arrives full of vigor at the threshold of adolescence. Frequently he elects to remain in the country, the proportion of children remaining in their adopted homes being from 35 to 55 per cent. Homes for the care of infants have been established and are visited every week by a physician and are under the daily supervision of a visiting nurse. The Institute accepts only children who are free from tuberculosis and other infectious diseases. The Paris Institute has been in existence for nearly eighteen years; 400 children are at present in its charge and more than 2000 have passed through its hands. A statistical study of 165 tuberculous families gives the morbidity from tuberculosis among children left in the care of their infected relatives as 60 per cent, without counting those in whom the disease remained latent. The mortality in [illegible] was nearly 40 per cent. Among the 2,000 children who have passed through the Institute at Paris there have been only 7 cases of tuberculosis, and of these 5 recovered. The moral transformation of the children is equally remarkable. The Grancher Institute has at Paris only a small office and two paid employees. The remaining expenses are insignificant. Before the war the complete unkeep of a child did not exceed 400 francs a year; since then the cost has risen to 1,000 francs. In the simplest sanatorium, the cost is not less than 15 francs a day. In three years the amount would be at least 20,000 francs, without the certainty of a complete cure. The Institute rescues a child from tuberculosis at a cost of from 3,000 to 5,000 francs. At Paris the Public Office of Social Hygiene of the Department of the Seine is endeavoring to extend the work of the Grancher Institute. An appeal is made to health authorities to undertake the fight against tuberculosis by this means, the efficacy of which has been so thoroughly demonstrated. In the absence of sufficient resources, the Grancher Institutes have not been able to expand to the extent desired. About 15 branches were in existence before the war. Tuberculosis relief committees are now endeavoring to establish them in all the departments of France. The United States, Belgium, and Italy have already commenced the organization of such societies for the protection of the children.—*The Grancher Institute: Its Rôle in the Campaign Against Tuberculosis, Internat. J. Pub. Health, ii, 115*

Tuberculous Children Sleep in Parks.—Tuberculous children from Westminister council schools have a class in St. James Park, London. In this class both health and education are considered. All the lessons take place in the open air, milk is provided for the children, and an hour's sleep is part of the daily routine. This siesta is taken in a sleeping bag on the park lawn, and serves not only to provide a beneficial rest but prevents the children from coming in contact with other children.—*News of the Week, Med. Rec., July 9, 1921, c, 73.*

The Results of X-Ray Treatment in Children.—Enlarged cervical lymph nodes are particularly evident in children. Isolated cases heal after 1 or 2 treatments, but the large indolent tumors require 5 o 6 radiations with an interval of three to four weeks, lasting in all about six months. The fibrous indurated types are not influenced. Fluctuating tumors are punctured and then rayed. Fistulae are not contraindications, except that the infected skin is hypersensitive to the X-ray. To prevent the inflammation from spreading one may also radiate the healthy nodes. No harm has been noted in any case. The X-ray works faster and with greater certainty than the quartz light. It influences diseased bones the more the smaller they are, especially in spina ventosa. In tuberculosis of the ribs and sternum, it is better to use the X-ray postoperatively. It is especially suitable in the treatment of peritoneal tuberculosis with palpable tumors. The pure exudative types heal just as quickly by other methods as by the X-ray. Harmful skin reactions are rarely seen, except in neuropathic children who are particularly susceptible to any type of ray. If the quartz light is used in conjunction with the X-ray, it is wiser to cover up the areas treated by the latter. Nontuberculous conditions treated without results were Hodgkins disease, tumors of the spleen, malignant tumors and hyperplasia of the thymus. Arthritis deformans was somewhat improved.—*Erfahrungen bei der Röntgentiefentherapie im Kindesalter, P. Karger, Jahrb. f. Kinderh., 1920, xciii, 5.*

The Treatment of Surgical Tuberculosis in Children by Venous Hyperemia.—In children the induction of venous hyperemia is not only quite equal to any other modern method of treatment of white swelling of the knee joint, with the exception of heliotherapy, but it is distinctly superior in many respects. The rapid allaying of pain is one of the first results when the procedure is properly employed. The bad position assumed by the involved limb improves spontaneously as soon as the pain disappears. The possibility of carrying out the treatment without the use of casts or other means of immobilizing the limb avoids the development of trophic disturbances of the skin, muscles and bone. Finally, when other therapeutic measures—always excepting heliotherapy—usually end in more or less complete ankylosis (which is even yet regarded as an ultimate aim), venous hyperemia preserves the joints as well as their movement, and this is not uncommon, but almost invariably the rule. Therefore, it should be given a high place in infantile surgical therapeutics in which conservative measures are all-important. Added to these advantages, treatment by venous hyperemia is absolutely inoffensive when rightly carried out. The accidents attributed to it are invariably due to a defective technique. Muscular atrophy at the point of application of the elastic band, chronic edema and, exceptionally, gangrene have been recorded, but they are always the result of a too tight application of the band. Acute suppuration in the sinuses or in tuberculous abscesses may also ensue from the ischemia caused by a too tight ligature and tuberculous lesions apear to be particularly aggravated by this ischemia or by an exaggerated edema whch produces a too intense or prolonged stasis. Consequently it is of utmost importance to watch for the slightest symptoms accruing from too energetic compression and to remedy this immediately. For this reason the simultaneous application of the elastic band and cups should always be avoided, as they produce an excessive stasis over the bacillary lesion itself. As to the manner of action of venous stasis one is reduced to hypotheses, each of which probably has a certain value, but no one taken singly is sufficient to give a satisfactory explanation. It must be admitted that the true *modus operandi* of the procedure still remains to be explained, but the numerous excellent—even exceptional—results plead in its favor. Its use is indicated at the onset of white swelling of almost any joint when the lesions are especially in the periarticular soft parts, and in osteitis with or without sinuses, when the bone lesion is superficial. Venous hyperemia can also be used to complete the results of a surgical interference on the bones Like all other conservative measures this one is contraindicated in very advanced tuberculous lesions of the bones and in rapidly developing osteoarthritis, when it is urgent to prevent the occurrence of visceral degeneration by resorting at once to a radical operation.—*Editorial, Mec. Rec., June 11, 1921, xcix, 1011.*

Combination Tuberculin Tests in Cattle.—Intracutaneous and ophthalmic tests should be applied in addition to the subcutaneous test, in diagnosing tuberculosis in a previously tested herd of cattle, or where the disease has prevailed for a number of years. By using all three tests the decision arrived at may be assumed to be 100 per cent perfect. It could easily happen in a herd of 40 animals to miss one by merely using the ophthalmic test; and, unless check tests were applied, a tuberculous animal might be left in the herd and spread the disease to healthy cattle. The ophthalmic sensitizing disc should be applied when the herd is first inspected, to be followed immediately by the intracutaneous injection. The second tablet can be applied after the forty-eighth or seventy-second hour observation has been made. For the intracutaneous test one standard place of injection should be chosen and care used in interpreting the local reaction. The latter is considered positive when an area of infiltration is formed, varying in size from a small pea to a quarter in diameter.—*Combination Tuberculin Tests, D. K. Eastman, J. Am. Vet. M. Ass., June, 1921, lix, 338.*

Intracutaneous Tuberculin Test in Cattle.—A syringe of 2 cc. capacity, with long, slender glass barrel and a leather or rubber plunger, or a 25 minim syringe with a gauge to regulate the dose, is recommended. The animal must be properly restrained so as to insure a perfect injection. Should the needle be dislocated, a new site, higher or lower or on the opposite side, should be chosen. The seat of injection is into the fold either right or left, but at a lower point than has heretofore been chosen. This is preferable because the skin here is denser and the subcutaneous or areolar tissue is less abundant. When a reaction occurs low, it is more distinctly circumscribed and more readily detected. For the injection, permit the tail, slightly below the point where the caudal fold passes gradually into the nude, smooth undersurface, to rest in the palm of the left hand, with the thumb resting against the left side of the tail, the hand at about an angle of 45 degrees, allowing the point of the index finger to press lightly against the undersurface slightly to the right. Press this tissue to be injected out to the right, which brings it into view, at the same time holding the second and third fingers in readiness to grasp the syringe as soon as the insertion is made. In making the insertion, be sure that the bevel of the needle touches the skin and is parallel with its surface. The amount of tuberculin to be injected should not exceed two minims. Should a greater amount be injected unintentionally, a notation must be made on the test chart, recording the number or name, in order that the animal may be identified when making the interpretations. If care is used in examining every questionable animal and ascertaining its history it will materially aid in making a diagnosis and rendering a decision.—*The Intradermic Tuberculin Test, O. Ausgpurger, J. Am. Vet. M. Ass., June, 1921, lix, 340.*

Tuberculin Test of Cattle and Tuberculosis Control.—In California, 300,000 cattle have been subjected to the intracutaneous test. In the hands of an experienced operator this test is not likely to give a positive reaction when animals are not affected with tuberculosis. The reaction, however, may appear later than the time ordinarily set for the observation. Other tests used are the subcutaneous, the sensitized intracutaneous, the intrapalpebral and the ophthalmic. The subcutaneous test is cumbersome, time consuming and not always accurate. The sensitized intracutaneous test consists in repeating the test at about the same location on the fourth day following the first injection. It is supposed to be more searching than the subcutaneous or the ordinary intracutaneous test. The intrapalpebral apparently has no points of advantage over the intracutaneous test. The ophthalmic test alone does not give as good results as the tests mentioned, but a modification of it known as the sensitized ophthalmic, repeating the test after two days with 2 discs, has recently gained in favor in detecting advanced cases of tuberculosis known as spreaders. These frequently cannot be found by any other means, except possibly by the use of the serological test which has not as yet been sufficiently used in common practice to determine its real value. Various tests used repeatedly may fail to check the spread of tuberculosis in some herds. If 80 per cent of cattle in a badly affected herd react to any test, one can be satisfied with the result. Among the remaining 20 per cent there are likely to be some of the most dangerous spreaders of the entire herd. This 20 per cent can be materially reduced by using a combination of tests. When spreaders are present in a herd and means of detection fail, the herd must be considered 100 per cent tuberculous. It is encouraging to note the great majority of cases that have remained free from the disease when herds have been placed on the accredited herd list by the United States Bureau of Animal Industry, after having been declared as free. This to some extent may be attributed to the fact that probably not a high percentage of accredited herds originally contained a high percentage of reactors. In one county, among a herd tested, not a single reactor was found, due to its geographical isolation. In another county, adjoining, where transportation and communication to the outside were easy, large numbers of tuberculous cattle were present. Practically nothing can be told from the physical appearance of an animal as to whether it will react to the test, but, given the history of a cow or herd, in a surprising number of cases the result may be predicted correctly. Dissemination is a potent factor. All that is necessary before making an intracutaneous test is to wipe the spot of injection clean. Unless the animal jumps, causing the needle to tear the skin, there need be no fear of infection. At a recent meeting of the United States Live Stock Sanitary Association at Chicago, a code for recording intracutaneous reactions was adopted. In California 20,000 tuberculous cows have been removed from raw milk dairies through the testing done under the pure milk law. It is estimated that about 5 per cent of the reactors are discharging tubercle bacilli at intervals or continuously through their milk. This means that, if it were not for the tuberculin testing done by the state, her unsuspecting citizens would be drinking raw milk from at least a thousand cows actually containing tubercle bacilli. To these should be added the other cows that would have contracted tuberculosis in dangerous form, had these 20,000 reactors remained in the raw milk herds. Add to this total the large number of cows that are spreaders in pasteurization herds which, but for the pure milk law, would be selling raw milk; and multiply this grand total by the milk from all healthy cows with which this contaminated milk from spreader cows would be mixed, and we have an enormous product of contaminated milk that cannot readily be grasped, but would include a great portion of our total supply of almost 63 million gallons annually.—*Some Observations Concerning Tuberculin Testing and Tuberculosis Control, J. J. Frey, J. Am. Vet. M. Ass., July, 1921, lix, 443.*

Tuberculosis of Horses.—This is generally considered of little economic importance, as of the thousands of horses which are autopsied annually, there are but few cases of tuberculosis reported. However horses, exposed to tuberculous cattle, may be a greater menace to livestock and public health than they have hitherto been regarded. For convenience we can divide horses into the unexposed and exposed. It is the exposed horse to which our attention should be drawn. This is by far the smaller group of the two, but of greater importance as regards tuberculosis. During the last two years 4 cases of tuberculosis in horses have been brought to the author's attention, all of which were exposed animals. At least 3 are to be classed as spreaders and the fourth, if not a spreader, was certainly dangerously near to that condition. To eradicate tuberculosis from herds continually exposed to such animals would be almost impossible. When we stop to think that these cases were all discovered as a result of their physical condition, one wonders how many cases might be found if special attention were given to this subject and all exposed horses tested with tuberculin. The author does not mean to recommend such a procedure, but rather to emphasize the fact that horses exposed to tuberculous cattle may contract the infection and become dangerous spreaders. Therefore, where conditions point to this possibility, exposed horses should be subjected to tuberculin tests.—*Tuberculosis of Equines and its Importance in Tuberculosis Eradication by the Accredited Herd Plan, F. Boerner, Jr., J Am. Vet. M. Ass., May, 1921, lix, 184.*

Prognosis of Pulmonary Tuberculosis.—An analysis of 300 incipient and moderately advanced cases shows that râles when present at the onset of treatment will, after from three to six months treatment, tend either to increase or diminish in more than half the cases. Only comparatively infrequently do they disappear or appear when previously absent. A fair number (about one in five or six) show no change in the area of râles heard. The roentgen ray will show no improvement in about one of seven cases, and approximately two-thirds will show definite improvement. Nearly three-quarters of the cases will show freedom from symptoms of activity. After from five to eleven years those patients in whom the râles increased in area while under treatment showed the highest mortality. When râles remained stationary during treatment, prognosis was not unfavorably influenced. Incipient or minimal cases have a better immediate and ultimate prognosis than the moderately advanced; moderately advanced a better prognosis than far advanced cases. Regardless of extent of lesion the cases becoming inactive under treatment have a much better prognosis than those which retain symptoms of activity. After the lapse of twenty years the cause of death was pulmonary tuberculosis in most of the traced cases. Those cases, which were inactive after treatment, have a better prognosis than those having symptoms of activity. Tubercle bacilli when present in the sputum make the prognosis much less favorable than when absent. This refers to longevity, general mortality and mortality from tuberculosis, and holds true for the incipient and moderately advanced cases.—*Prognosis of Pulmonary Tuberculosis, F. H. Heise, Canad. M. Ass. J., May, 1921, xi, 314.*

THE

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ABSTRACTS OF TUBERCULOSIS

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The Abstract Editor is Dr. George Mannheimer, 41 West 51st Street, New York City. Prompt transmission to him of reprints or abstracts of papers on tuberculosis, sanatorium or board of health reports, etc., will promote their early publication in this section.

Abstracts should be sent typewritten on one side of the page only. They should be as concise and compact as the subject matter of the article warrants. They should be headed with a short title, and followed by the full title of the paper, author's name, journal, date, volume and page.

History of Tuberculosis.—References to pulmonary tuberculosis under the name of phthisis are found in the earliest medical records; and Hippocrates and Galen gave excellent clinical descriptions of advanced cases. Hippocrates defined phthisis as suppuration and ulceration of the lung; and included empyema, bronchiectasis, abscess of the lung and gangrene under the same head. Franciscus Sylvius (1614–1672) gave the main symptoms of the disease, such as wasting, cough, spitting of pus and hectic fever. He attributed the disease, in most cases, to pleurisy ending in suppuration. While Hippocrates and his successors had observed only cavities, Sylvius stated that tubercles are often seen in the lung in cases of consumption, and that these may soften and form vomicae. He thought that tubercles are enlarged lymphs nodes and that these nodes become visible when diseased. Richard Morton (1635–1696) observed that the disease is very prevalent, that it associated with lymphatic swellings elsewhere, and that tubercles are found in the lungs in all cases of consumption and often heal spontaneously. Matthew Baillie (1761–1823) observed that there are no lymph nodes in the lungs and that tubercles arise in the cellular tissue. Bayle (1774–1816) was the first to use the word miliary and tuberculous diathesis. Laennec (1781–1826) stated that all phthisis is tuberculous. Virchow (1821–1902) pointed out that not caseation, but miliary tubercle is the criterion of tuberculosis. In 1868 Villemin published his work on the experimental production of tubercle in animals. In 1882 Koch announced his discovery of the tubercle bacillus. For two thousand years the disease was regarded as incurable, until in modern times series of necropsies from general hospitals were published, when about 80 per cent of bodies were found to contain arrested tubercle, in the lungs or elsewhere. The hereditary factor had been regarded as the chief cause until modern times. The treatment had been warmth, suitable climate and blood letting. In 1840 the author's grandfather introduced the use of codliver oil. Open air methods were introduced about 1850, though Sydenham in 1670 recommended horseback riding. Brehmer started the first sanatorium in Germany in 1859.—*The History of Tuberculosis, H. E. Symes-Thompson, Practitioner, June, 1921, cvi, 426.*

Framingham Community Health and Tuberculosis Demonstration. — The Framingham Community Health and Tuberculosis Demonstration has been in active operation now for more than four years. Although the time is too short completely to evaluate the results, most of the medical work is being done through the consultation service, at the request of physicians, and the results that have been obtained have been due to the coöperation of the physicians. The amount of tuberculosis discovered in the early part of the demonstration, through all channels, indicated that 1 per cent of the people had active pulmonary tuberculosis. The average number of tuberculosis cases reported to the board of health in Framingham in the decade before the demonstration started was thirteen per year. During the last four years, the average number of cases reported to the board of health has been forty-three per year. At the present time (June, 1921), the number of active tuberculous cases is considerably less than at any time since the demonstration started. In the diagnosis of tuberculous disease, in all cases that have been seen by the community demonstration examiner, the diagnostic standards covering pulmonary and nonpulmonary disease in childhood and adults, were prepared for the demonstration by a committee appointed by the president of the National Tuberculosis Association. Since the demonstration opened, there have been eighteen deaths that, after careful analysis of their histories, it would seem should have been prevented or at least postponed. This number represents 19 per cent of the total number of deaths analyzed since the demonstration opened. During the four year period, out of a group of 376 individuals, including active, arrested, early and advanced disease, 21 per cent died. Those whose deaths were classified as preventable or postponable constitute 4+ per cent. Consequently, the percentage of the total that might be considered to represent the irreducible fatality rate for such a representative group of tuberculous individuals over a period of four years would be 21 per cent minus 4 per cent, or 17 per cent. The chief factors that seem to be responsible for the late discovery of tuberculosis cases which give to the community every year advanced and dying patients that have not been known or treated for tuberculosis in the early stages of the disease are the recluse type, which seems to be the main type, never receiving any medical attention; failure of patients to seek medical advice early, or, if they do, not to give the physician sufficient time to make a diagnosis; occasional failure of physicians to detect disease early; failure of both physician and patient to use all of the services at their command for early diagnosis of tuberculous disease; lack of complete annual medical examination; and lack of annual factory and school examinations.—*Framingham Community Health and Tuberculosis Demonstration: Certain Medical Results, D. B. Armstrong and P. C. Bartlett, J. Am. M. Ass., August 20, 1921, lxxvii, 585.*

Fundamental Factors in the Control of Tuberculosis.—The campaign for the control of tuberculosis is one of education and not of quarantine. It must extend over a long period of time and on a big scale. It must take cognizance of the fact that as the disease decreases, the fight must be more carefully made, because our race becomes one of nonimmunes. It will require constantly increasing sums of money, which must be secured from the public. It can be secured only by keeping in touch with the people, to insure their coöperation. To do this the workers must not travel too far ahead of public sentiment, nor forget public ideals. No campaign can be successful unless it is a part of a general health movement, coördinated with the various bureaus of the health department, subservient to the general health movement, and coördinated, further, with all welfare agencies and the Bureau of Animal Husbandry. The educational system must include the extension department of the bureau, keeping in touch with the tuberculous population, presented to them in their own language, catering to their ideals, and to local and sectional peculiarities. The sanatorium is the fountainhead from which all this should flow and through which public sentiment for the final work may be crystallized. The sanatorium is a failure, as far as the prevention of the disease is concerned, unless it is operated as an educational institution rather than as a hospital. A place must be had where the indigent tuberculous population may be cared for during the remaining days of their lives, in order to protect an increasingly large number of the nonimmune race from the dangerous carrier.—*Fundamental Factors in the Control of Tuberculosis, with Especial Reference to the Sanatorium, H. Boswell, J. Am. M. Ass., August 13, 1921, lxxvii, 523.*

Sanatorium Care of Tuberculous Soldiers.—The authors discuss the tuberculosis problem which has arisen from the war and which the federal government is trying to solve. They report on the results of an inspection of tuberculosis sanatoria and the work being done and point out the needs of this service. One of the most serious obstacles in the operation of government sanatoria is the scarcity of physicians and nurses specially trained in tuberculosis. Theoretically, many of the government sanatoria are too large to attain the maximum of service for the individual patient. On account of the shortage in medical personnel, it has been found impossible to secure entirely satisfactory commanding officers and chiefs of medical service for all of the existing institutions. The most serious fault in these government sanatoria, and one which will be overcome only with the greatest difficulty, if at all, is the flagrant lack of discipline to be observed in practically all of the institutions. The patients apparently fail to recognize that reasonable discipline is an essential part of the treatment of tuberculosis, and seem to regard all disciplinary efforts as an arbitrary and offensive use of authority. It was the opinion of every member of the inspecting committee that the men are being distinctly harmed by the possession of an excessive amount of money derived from federal compensation, and it was recommended that some legislative action be taken by Congress, whereby compensation funds may be turned over to the members of the soldiers' families or accumulated with interest until the soldier is discharged from the sanatorium. So long as these restive and restless patients feel that their insubordination and hurtful indiscretions are condoned, and so long as the authority of the institutional heads is overridden by powerful political influence, government sanatoria will fail to measure up to any sort of high standards and will fail to compare favorably with well conducted private institutions. If every physician and every nurse connected with the government sanatoria are required to become proficient through special training and instruction, there will ultimately be available a large group of physicians and nurses who will find ready employment and who will be exceedingly valuable in the many county and municipal sanatoria which are being established in all parts of the country.—*The Sanatorium Care of Tuberculous Soldiers by the Federal Government, G. T. Palmer and H. W. Hoagland, J. Am. M. Ass., August 13, 1921, lxxvii, 506.*

Smoking in Pulmonary Tuberculosis.—The circulatory stimulation of tobacco is decidedly advantageous to some patients. One patient stated that smoking caused his temperature to rise. Investigation verified his assertion. In habitual smokers tobacco increases pulse rate and, to a certain extent, the blood pressure. As a result of this circulatory stimulation, there occurs an increase in the movement of the blood which is shared by the pulmonary circulation. In this respect, the effect of smoking is analogous to that of exercise. It is obvious that this increased flow of blood through the lungs can only favor the access of toxins to the circulation, certainly undesirable if sufficient to cause a rise in temperature. It is also evident from the foregoing that smoking should be stopped by those patients with bloody expectoration or recurrent hemorrhages. This effect of tobacco does not occur in every individual. Some patients may smoke without ill effect; but in any case in which the question arises whether or not smoking is inadvisable, decision can be made only by observation of the effect of tobacco on that particular individual. In other words, the effect of smoking deserves investigation in every case.—*Smoking in Pulmonary Tuberculosis, E. A. Duncan, J. Am. M. Ass., August 13, 1921, lxxvii, 526.*

Tuberculosis after Industrial Accidents.—Broca recalls that there is a history of visceral or glandular tuberculosis in practically every case of tuberculous lesions in bones or joints. On the other hand, tubercle bacilli are very rarely found in the blood in the chronic tuberculous. Still another argument against the traumatic origin of bone and joint tuberculosis is his discovery that none of 500 children whom he has treated for contusions, sprains or other trauma before 1913 has developed a tuberculous process since in the region of the injury. The industrial accident which every one is so prone to hold responsible for the tuberculous lesion in reality probably merely revealed its unsuspected presence. The movement which reveals the pathological condition may not be greater or more vigorous than the ordinary movements, although claimed as trauma by the subject. Two important practical conclusions are evident from his data. One is that every accident involving a bone or joint should be radiographed immediately; this would do away with the necessity for much litigation. The other conclusion is that any history of a tuberculous bone or joint affection should exempt from military service, with its right to a pension, for any affection declared or aggravated later than sixty days after being enrolled.—*Note sur la tuberculose ostéoarticulaire des accidents du travail, A. Broca, Bull. Acad. d. Méd, May 31, 1921, lxxxv, 629.*

The Phrenic Sign in Pulmonary Tuberculosis.—Ragot has been impressed with the constancy of a very sensitive point in the supraclavicular fossa with pulmonary tuberculosis. The pain on pressure is diffuse and extends deep into the middle of the chest. The point in question is where the phrenic nerve lies on the anterior scalenus muscle, between the two heads of the sternocleidomastoid. Pain on pressure here is a very early sign of tuberculous infection of the lung, and seems to be constant with this, but is never found with pneumonia or other nontuberculous processes.—*Le signe du phrénique dans la tuberculose pulmonaire, A. Ragot, J. d. Méd. d. Bordeaux, May 25, 1921, xcii, 272.*

Albumin in Sputum Aid in Early Diagnosis.—The qualitative and quantitative examination of the sputum for albumin is an easy and useful method of arriving at a diagnosis in the earlier stages of pulmonary tuberculosis, and might with advantage be employed not only by the specialist, but also by the busy general practitioner. The presence of albumin in the sputum is an indication of active disease of the lung tissue itself. If the bronchi alone are affected, the amount of albumin present, if any, will be negligible. If other inflammatory diseases of the lungs are excluded, all patients with 0.2 per cent or more of albumin in the sputum may be regarded as suffering from active pulmonary tuberculosis. Used in conjunction with diagnostic subcutaneous injections of a reliable tuberculin, the albumin test is a means of distinguishing between active and inactive tuberculosis. If the reaction is positive, the disease is active; if negative, the condition is latent.—*Significance of Albumin in Sputum; Application to Early Diagnosis in Pulmonary Tuberculosis, A. C. Alport, South Afr. Med. Rec., April 9, 1921, xix, 127.*

Stability Reaction of Blood in Tuberculosis.—If blood is prevented from coagulating (for instance, with oxalate or citrate), the red blood corpuscles during gravidity and in most pathological states sedimentate faster than in normal conditions. Westergren has investigated the suspension stability as it occurs in pulmonary tuberculosis. Altogether about 4,000 tests have been made. It is obvious that a reaction of the organism caused by the pathological process (proceeding or just passed off) is reflected in the suspension stability of the blood. And, furthermore, the degree to which the stability is reduced corresponds surprisingly well to the extent of activity which the process, clinically interpreted, may be presumed to possess. On the whole, the figures are increased with increase of lesions of the lung tissue, but acute cases show the strongest reactions, and chronic cases relatively lower figures, which are generally correlative to the activity of the process. No single test of an active, or probably active, case has given a normal value, and no case which must be considered quite benign and certainly shows no signs of activity, has given a high, even a middle-high figure. The stability frequently is reduced, even to a very high degree, though for a long time quite a normal temperature has been observed, and the stability reaction seems considerably more than the temperature to be a reliable measure of the activity of the process. When a series of probatory injections of tuberculin was made, and the patients were followed up with stability reaction tests every day or every second day, without exception a typical influence by the tuberculin on the stability has been discovered; in the first place, an obviously increased sedimentation appears, which may be noted earlier and always lasts for a longer time than the reaction of the organism which is manifested in the general state and by careful measurements of the temperature. Though reduction of the suspension stability is in no way a specific reaction, the stability reaction very likely can have a diagnostic value for tuberculosis. With normal stability, an active phthisis is most probably to be excluded.—*Stability Reaction of Blood in Pulmonary Tuberculosis, A. Westergren, Brit. J. Tuberc., April, 1921, xv, 72.*

Complement Fixation in Surgical Tuberculosis.—Contrary to the usual opinion that humoral antibodies are found only in visceral tuberculosis, the authors find a large percentage of cases of tuberculosis of the bones reacting positively with Besredka's antigen. Eight hundred and sixty-nine cases of bone, joint and lymph node disease, including 713 cases of tuberculosis of vertebrae, hip, knee, etc., were examined. Ages varied from two to fourteen years. In general, positive reaction was indicative of activity of the lesion. Where the process was beginning to be limited by fibrosis, the reaction was usually negative. Of 100 cases of rickets examined, 10 gave positive complement fixation tests with the Besredka antigen. Six per cent of 56 other cases of nontuberculous bone disease reacted positively.—*Réaction de fixation a l'antigéne de Besredka dans la tuberculose externe, B. Fried and M. Moser, Ann. de l'Inst. Pasteur, June, 1921, xxxv, 388.*

Complement Fixation Reaction in Tuberculosis.—Seventy-seven out of 78 cases of manifest pulmonary tuberculosis gave positive complement fixation tests with Besredka antigen. The single negative result occurred in a patient dying with tuberculous pneumonia, who had syphilis at the same time. Four out of 6 cases of tuberculous peritonitis reacted positively. Of the 2 negatives one died of tuberculous meningitis, and the other was in a state of profound cachexia. Sixteen out of 28 cases of serofibrinous pleurisy, presumably tuberculous, reacted positively, as did 20 out of 44 cases of tracheobronchial adenopathy. The reaction was positive in 51 out of 80 cases of clinically latent tuberculosis. Of 148 cases where tuberculosis was not believed to be present 17 reacted. The 131 negative ones included a number of nontuberculous respiratory diseases. Positive results were secured in some cases with the blood of syphilis and malaria patients. Except in the presence of these diseases the authors consider the reaction highly specific.—*Réaction de fixation (antigène de Besredka) et tuberculose, J. Rieux et Mlle. Bass, Ann. de l'Inst. Pasteur, June, 1921, xxxv, 378.*

Disinfection of Tuberculous Sputum.—In order to be of general use a tuberculous sputum disinfectant should be cheap, nonpoisonous and odorless, and disinfection should be simply and rapidly performed. On account of the difficulty of penetration of sputum masses a homogenizing agent like antiformin seems essential. The latter is, however, too expensive. Tests with sodium and potassium hydroxide in various concentrations proved unserviceable since they require shaking or agitation. Their caustic action also excluded them. A double volume of milk of lime (20 per cent), shaken before use, proved a good homogenizing agent, homogenizing even large lumps of sputum within one hour. After standing for some time the majority of the tubercle bacilli in the sputum were found in the upper layers of fluid. To the homogenized sputum was then added enough unslaked lime in small lumps (walnut size) until they could be seen at the fluid level. A violent reaction occurs sufficient to occasion a temperature of 100–102°C. which then gradually drops, but remains over 95° for five minutes, that is, sufficiently long to kill tubercle bacilli. The best proportion of unslaked lime to milk of lime was found to be 2:1. Pulverized unslaked lime was not as serviceable as the lumps of walnut size since the reaction became too violent. Mixtures of lime with sand or magnesium salts were not as serviceable. The unslaked lime must be kept in closed vessels and tested before use with water, using 200 grams of unslaked lime to 100 cc. of water. A temperature of 100°C. must be reached within the first twelve minutes. *Instructions*: Water is put in the sputum cup and an equal volume of sputum is deposited. For disinfection the cup is placed on news or blotting paper, and unslaked lime is added until about as much is visible above the fluid as is contained below it. At the end of disinfection, which is accompanied by the evolution of heat and steam, the entire mass is allowed to cool and is poured (now being harmless) upon a sheet of paper which can be thrown upon the waste pile. The cup can be further rinsed with warm water. With tenacious sputum it is advisable first to use an equal volume of milk of lime (100 volumes of unslaked lime mixed with 60 parts of water; of the resultant powder 1 litre mixed with 4 liters of water).—*Über die Desinfektion des Tuberkulösen Auswurfs, Schuster, Ztschr. f. Hyg., July 6, 1921, xcii, 510.*

Antigenic Property of Low Virulent Tubercle Bacilli, Turtle and Other Acid fast Bacilli.—Reasoning that the allergic reaction is the first and foremost earmark of an immunity in tuberculosis, the antigenic (sensitizing) properties of four different strains (Valleé's low virulent tubercle bacillus, an avian tubercle bacillus, a grass bacillus and Friedmann's turtle bacillus), of living bacilli in doses of 1 to 100 mgm., were tested by injection intraperitoneally in guinea pigs. After an incubation period of twenty-three to thirty-two days an exciting intravenous injection of 50 mgm. of heat-killed human tubercle bacilli was given to the majority of the 29 pigs tested. Of the turtle and grass bacillus prepared pigs one was tested with old tuberculin (0.5 cc. intraperitoneally) and 3 with 50 mgm. of bacilli of the homologous strain intravenously, to determine whether sensitization to the same strain was more successful than to the human bacilli. The grass and turtle bacilli proved only slightly if at all antigenic (sensitizing), while the Valleé and avian strain fairly consistently proved antigenic; both of the latter regularly producing tuberculous changes in the organs in doses of 1 and 10 mgm. The conclusions reached are that the Valleé and avian bacilli in large disease-producing doses fairly regularly act as antigens, while the grass and turtle bacilli even in very large doses are practically without antigenic properties, thus resembling dead bacilli. They lack the power to produce disease upon which the sensitizing and immunizing action of living bacilli depends.—*Beitrag zur antigenen Wirkung von schwachvirulenten Tuberkelbazillen, Schildkröten- und anderen säurefesten Bazillen, Fürth, Zschr. f. Hyg., December 13, 1920, xci, 197.*

The New Concentration Methods for Examination for Tubercle Bacilli in the Sputum.—The author reviews the recent reports from laboratories doing large numbers of microscopic examinations for tubercle bacilli in the sputum and his own personal experience with the following methods: the simple antiformin (one part of sputum and two parts of 50 per cent antiformin); the Schulte procedure (the former mixed with one part of alcohol); the iron chloride precipitation of Ditthorn-Schultz (six parts of the second mixture with 0.3 part 20 per cent ferric chloride solution); and the aluminum sulphate method of Schmitz-Brauer (six parts of sputum with 0.3 part of 10 per cent aluminum sulphate solution and a few drops of equal parts of absolute alcohol and chloroform). Since approximately only 20 per cent of sputums sent to laboratories are found positive by the ordinary direct staining method, to examine all of the remaining 80 per cent of negative sputums by the special methods entails too much work. It is therefore recommended that sputums, as sent in for examination, be studied in the original smear. If this is negative, it is so reported and a request for a second sample is submitted with the report. The second specimen, if negative in the original smear, is then submitted to the antiformin test (Uhlenhuth), preferably the simple procedure. Sputums which yield only small amounts of sediment by this method are subjected to procedures which precipitate the proteins present. In this way time is saved which may be well spent in the examination of sputums demanding special attention.—*Die neueren Anreicherungsverfahren für den Tuberkelbazillen—Nachweis im Sputum und ihre Anwendung bei den Untersuchungsämtern, F. Friedland, Ztschr. f. Hyg., January 29, 1921, xci, 440.*

Pseudotuberculosis Due to Disease of the Upper Air Passages.—During the late war the French physicians had considerable to say of a false tuberculosis encountered in recruits, which very closely simulated the genuine condition but was found to improve on the correction of intranasal deformities, sinus disease, and other anomalies of the upper air and food passages. In the *Journal de médecine et de chirurgie pratiques* for March 25, 1921, cviii, 6, Festal gives an elaborate account of the syndrome in question. The author states that it was well enough known before the war, but that the latter focused the eyes of the profession on it. Sergent found that many subjects rejected as tuberculous or suspects were of this type, which was moreover very common. The resemblance to the early stage of tuberculosis of the lungs was often startling—slight temperature rise, emaciation, lassitude, spasmodic cough with profuse expectoration in the morning on waking, and even physical signs suggesting apical lesions. Of the two resources which might be expected to diagnosticate or exclude tuberculosis even the X-ray seemed noncommittal; only the bacteriological examination was frankly negative. The X-ray plate showed at times the absence of normal transparency of the apex with or without a suspicious hilum shadow. Auscultation and percussion gave the signs commonly encountered in early apical tuberculosis, such as lessened breathing, prolonged expiration, and slight dulness. The research for Koch's bacillus continued to be absolutely negative in the face of all subtleties of resource for bringing out the latter. In the course of a systematic examination the patients were found to present nasal obstruction, hypersecretion from the nasal passages which was at times purulent, empyema of some one or more of the sinuses, adenoid hypertrophy, and in some cases atrophic rhinitis. The patients attributed these troubles to tobacco and so were not especially concerned about them. Indeed, they seem to have given them very little inconvenience. The rhinologist in examining these cases learned to look into the nasopharynx at the outset and the peculiar conditions encountered there sufficed to exclude for the time the suspicion of tuberculosis. There was, however, always the possibility of supervention of the latter. Lemoine and Sieur once placed on record the physical signs encountered in the lungs of mouth-breathers irrespective of the causation. These sufficiently resemble those of beginning tuberculosis, and the author frankly admits that he does not attempt to differentiate by physical signs alone. One should proceed at once to the bacteriological diagnosis, but should this prove negative one cannot always straightway exclude tubercle. Difficulty of radiological differentiation has already been mentioned, and the reliance on the effects of treatment of the nose and nasopharynx. But while in one patient the change for the better is at once apparent, in another two or three months may elapse before the benefit is realized. There is a third type in which, after a clearing up of the upper passages, the patient's chest shows no improvement at all, and here we have to regard him, for the time being, as actually tuberculous or perhaps as having recovered from tuberculous lesions with residual sclerosis, etc., until time comes to our aid.—*Editorial, Med. Rec., August 27, 1921, c, 372.*

Laryngeal Tuberculosis.—Careful investigators differ widely as to the number of tuberculous patients who develop a laryngeal complication. Its occurrence, however, is much more common than is ordinarily supposed. Baldwin of Saranac Lake reports an involvement of the larynx in from 16 to 40 per cent of his cases. Von Ruck gives 58 per cent. Lockard from a collection of 14 reports gathered from different parts of the world estimates the average as 34.5 per cent. Mullen says the percentage varies from 5 to 85 per cent, but thinks the latter figure to be more nearly correct. The author believes 40 to 50 per cent of all pulmonary cases have laryngeal involvement. The disease is much more prevalent in men than in women, the proportion being 3 to 1, and it most commonly occurs between the ages of twenty and forty. The etiological factors are irritation of the larynx due to inhalation of smoke and dust, strain and a lowered general resistance. The three sources by which the bacilli may reach the seat of the lesion are the blood, lymph and sputum. Blood and lymph as avenues of infection give rise to deeper infiltrations in the submucosa. Infection through the sputum, when it occurs, is found most frequently in advanced cases. These lesions are more superficial. Primary tuberculosis of the larynx is a mooted question. Baldwin says there is one primary case on record. Lockard questions the existence of any primary case. Dworetzky has classified the lesions of the larynx into acute, subacute and chronic. Pathologically, the active lesions of the larynx are usually described as consisting primarily of local anemia followed by congestion. This, in turn, is followed by infiltration, and finally an ulcer occurs on the site of the original anemia. The primary anemia is rarely seen and a slight congestion is more often the initial lesion. About one-third of the early laryngeal cases show no symptoms and the diagnosis of tuberculosis depends upon the laryngoscopic examination and a familiarity with the normal larynx. The frequency of involvement of the various parts of the larynx is in most instances directly proportional to their exposure to irritation and functional activity. Care must be exercised in differentiating catarrhal laryngitis, syphilis, and malignant or benign growths. The disease is curable at any stage. Unless complicating a hopeless lung condition, the tendency of all early cases is to become clinically well. With the appearance of late symptoms and signs the outlook is grave but not hopeless. Some of these cases will make remarkable improvement. The most important thing to remember is that the condition is an evidence of a general lowered resistance. The primary focus must be sought and treated. For the laryngeal lesion the treatment is both preventive and curative. Institutional care for laryngeal patients is important because of the influence of environment and the opportunity offered for detailed supervision and control. Careful and frequent examinations of the larynx in all cases of tuberculosis are urged. When lesions are found, the cough, as far as possible, is to be suppressed and controlled and the patient impressed with the fact that he must rest physically and mentally. In the treatment of the active tuberculous lesions of the larynx, the control of the use of the voice is perhaps 75 per cent of the essential treatment. The throat may be kept clean by the use of alkaline sprays. For the relief of the cough various oils may be used in the vaporizer or intratracheal dropper, or administered by direct intratracheal injections. Sluggish lesions, especially ulcers, may be stimulated to heal by the direct application of formalin, lactic acid or argyrol. In more severe cases, pain may be relieved by insufflation of powders, such as orthoform and anasthesin. Cocaine should be reserved to the last. Surgery has a very limited but useful field. Where the lung condition is quiescent the use of the X-ray and tuberculin to stimulate healing are recommended by some. Sunlight, directly reflected upon the diseased areas by means of the Verba instrument, seems to have especially beneficial results. The general practitioner is urged to become familiar with and make frequent use of his laryngoscope.—*Laryngeal Tuberculosis; Deductions from Study of 400 cases in Stonywold and Tucson, Arizona, Sanatoriums, E. W. Hayes, Southwest. Med., August, 1921, v, 1.*

Tuberculosis of the Middle Ear.—This study includes 200 cases of purulent otitis media, all but one of which had a mastoid operation performed. Tissue removed at the time of operation was examined, and guinea pigs were inoculated with the exudate. Of the 200 cases 20 were found to be tuberculous, most commonly in children between one and ten years of age. Contagious diseases of childhood are undoubtedly of etiological importance. The presence of multiple perforations is considered to be of little diagnostic value. Observable tubercles in the drum head are rare. A feature of importance is the presence of abundant and rapidly recurring granulations in both acute and subacute tuberculous otitis. The appearance of a cold abscess in the region of the ear points to a tuberculous infection of the mastoid process. Facial paralysis is to some degree characteristic of grave cases, but in general this sign is not common. The finding at operation of a putty-like matter, the color of which is yellowish white or grayish white, is believed to be actual proof of the presence of tuberculosis. Out of Leegaard's 25 cases, 12 began with an acute otitis, two of these with slight pain. In the tuberculous patient the wound after a mastoid operation may require six months to a year to heal. Tuberculin was used locally in 9 cases; 4 of these were cured, 3 improved, 1 doubtful and 3 unimproved. The bacteriological investigations proved all strains to be of the human type.—*Tuberculosis of the Middle Ear, F. Leegaard, Laryngoscope, June, 1921, xxxi, 374.*

Axillary Lymph Node Tuberculosis in Pulmonary Tuberculosis.—An examination of 40 cases of pulmonary tuberculosis for the presence of tubercle bacilli or anthracosis in the axillary lymph nodes revealed without question in 20 of them a connection between the diseased lung and the axillary nodes of the same side. In all the positive cases there were widespread adhesions between the pleural surfaces, while associated axillary node disease was never found in the absence of pleural adhesions; neither was it found in cases without tuberculosis in the lung. In the 20 positive cases, 15 revealed tuberculous nodules in the axillary nodes, 6 of which had also anthracosis, and 5 had anthracosis without tuberculosis. Tuberculous involvement of the mammae, external chest wall, or upper extremity was found in no case. Tattoo marks were absent in all cases. *Conclusions*: 1. Axillary node tuberculosis in the absence of external portals of entry indicates disease of the lung. 2. Isolated axillary node tuberculosis, even in the absence of clinical pulmonary findings, should suggest a latent pulmonary tuberculosis. 3. Combined carcinoma and tuberculosis of the same axillary glands are explicable on the basis of the presence of carcinoma of the mamma or upper extremity with a latent pulmonary tuberculosis.—*Tuberkulose der axillaren Lymphknoten bei Lungentuberkulose, Pickhan, Virchow's Arch. f. Path. Anat., April 9, 1921, ccxxxi, 212.*

Tuberculous Edematous Infiltration of the Lung.—Pulmonary edema in certain cases plays an important rôle in the evolution of acute bronchopneumonic tuberculosis. The edematous tuberculous infiltration has a relatively slow course, its macroscopic appearance resembles that of Roquefort cheese and its pathogenesis lies in the reactivation of a chronic tuberculosis. The clinical findings are flatness on percussion, disappearance of fremitus and egophony. Radioscopy reveals an opaque shadow. Repeated thoracenteses at different levels and on different days reveal a serous fluid on deep puncture. This fluid contains seroalbuminous droplets, pulmonary cells, pus cells and no organisms. Sputum is at first scant. Later it reveals tubercle bacilli, usually only during the last few weeks of the illness. A case is reported in detail illustrating the points stated.—*Infiltration oedémateuse tuberculeuse du poumon, G. Caussader and E. Doumer, Progr. Méd., May 21, 1921, no. 21, 225.*

Unusual Cases of Abdominal Tuberculosis.—The first case is that of a male infant of five months who had been ill for eleven days with diarrhea and vomiting. The abdomen was tender, markedly distended and showed dulness in the flanks. The pulse was rapid and feeble and the temperature 102°. Laparotomy showed free pus and intestinal contents in the peritoneal cavity, a perforation of an intestinal ulcer and a mesenteric abscess. Autopsy showed extensive tuberculous ulceration of the small intestine. One of the ulcers had perforated and the cavity of the mesenteric abscess was in relation to a ruptured tuberculous caseating lymph node. The unusual points about this case are the age of the patient and the presence of the solitary, well marked abscess originating in a tuberculous mesenteric node. The second case is that of a male of thirty-four years who gave a history of pain in the left iliac fossa for three weeks. A tender mass was felt there. On laparotomy an abscess containing foul smelling sterile pus was found, the wall of which was bounded by mesentery and bowel. From the wall a semicalcareous lymph node was removed which undoubtedly gave rise to the abscess. A few calcareous nodes were felt elsewhere in the mesentery.—*Two Unusual Cases of Abdominal Tuberculosis, E. G. Slesinger, Brit. M. J., May 14, 1921, no. 3150, 703.*

Renal Tuberculosis and Impacted Pelvic Calculus.—The differential diagnosis between renal lithiasis and renal tuberculosis, while relatively simple, in many cases may be extremely difficult or impossible without exploratory operation. Roentgenographic examination is the most valuable aid in differentiating between the two conditions. The case of a woman of thirty-seven who had had several attacks of renal colic and twice an operation for removal of kidney stones is reported. She had influenza in 1918, following which she lost considerably in weight. She complained of pain in the right iliac fossa. A large mass was felt in the upper right quadrant. The catheter met with obstruction on the right side. A stone was seen on that side on the X-ray plate. At operation a large grayish stone was found. The kidney was markedly enlarged and contained multiple tuberculous abscesses. Probably the calculus formation preceded the tuberculous infection.—*Tuberculosis of the Kidney Complicated by Impacted Pelvic Calculus, H. A. Fowler, J. Urol., April, 1921, v, 345.*

Medical Management of Renal Tuberculosis.—*Conclusions*: 1. Let practitioners and internists take heed early of symptoms suggestive of an incipient and developing tuberculosis of the kidney. Prompt use of every available means of diagnosis should be employed, to the end that early diagnosis may be established. 2. When unilateral tuberculosis of the kidney is proved to exist, nephrectomy offers the shortest and surest road to recovery. Dallying with such cases is inexcusable. 3. There is substantial reason for believing that earlier diagnosis in this, as in pulmonary tuberculosis, and the faithful and intelligent application of proper treatment—rest, hygienic, dietetic and therapeutic measures—may enable arrest or cure of the disease. But this plan should never supplant surgical intervention when there is proved unilateral tuberculosis of the kidney or there is evidence of retrogressive changes.—*Renal Tuberculosis; its Early Recognition and Management from the Viewpoint of the Internist, F. B. Wynn, J. Indiana State M. Ass., February, 1921, xiv, 33.*

Differential Diagnosis of Renal Tuberculosis.—Tubercle bacilli in the urine from a diseased kidney mean tuberculosis on this side. Their absence does not eliminate the disease. Cystoscopy and ureteral catherization are of value in the obscure case and necessary in every case coming to surgical treatment. Not infrequently repeated examinations are necessary, and a differential diagnosis may take many weeks, occasionally many months, or may rest upon a justified surgical exploration.—*Renal Tuberculosis; Its Differential Diagnosis, H. O. Mertz, J. Indiana State M. Ass., February, 1921, xiv, 35.*

Pathology of Renal Tuberculosis.—Tuberculous infection reaches the kidney from a neighboring focus, by way of the lymphatic system, by the bloodstream, and by ascent from the bladder via the ureters. The latter is the most important avenue of infection. Out of every 5 cases of active tuberculosis 1 case on the average will have renal tuberculosis. The following types of involvement are met: (1) miliary tuberculosis, one of the manifestations of generalized tuberculosis and (2) the caseous or caseocavernous type which begins at one papilla and spreads peripherally, or an abscess breaks into the pelvis. It is progressive and in 55 per cent limited to one kidney.—*Renal Tuberculosis; Its Pathology, V. H. Moon, J. Indiana State M. Ass., February, 1921, xiv, 38.*

Roentgen Diagnosis of Renal Tuberculosis.—*Conclusions*: 1. The use of the X-ray in diagnosing renal tuberculosis is new and is not yet appreciated. 2. By the use of filters and different penetrations a series of films of different densities of the entire urinary tract should be made in all suspected cases of renal tuberculosis. 3. One out of 5 cases of renal tuberculosis will show definite roentgenographic signs. Other methods of diagnosis may have failed and the X-ray alone may diagnose it. 4. Proper illumination in the study of the films is of the utmost importance. The shadows found are caused by the deposit of calcium in the tuberculous area. They may vary from small indefinite punctate areas to the characteristic lobulated mottled shadow which is typical of a completely destroyed kidney. 5. Preparation of the patient for the examination is very important. 6. Pyeloscopic and pyelographic examinations are of value in early inflammatory infection of the kidney. 7. Cystograms of air and opaque solutions are helpful in showing bladder conditions.—*Renal Tuberculosis; Value of Roentgenographic Diagnosis, R. C. Beeler, J. Indiana State M. Ass., February, 1921, xiv, 40.*

Surgical Treatment of Renal Tuberculosis.—In unilateral renal tuberculosis early nephrectomy is indicated, and affords the only assurance of cure. When both kidneys are infected nephrectomy is contraindicated, unless one is practically destroyed and the other still has good functional capacity. Urinary symptoms usually persist after operation in proportion to their duration before the operation. Under tuberculin treatment, with proper dietetic, climatic and hygienic management, many cases will be improved, but are likely to have recurrences later. Seventy-five per cent of unilateral renal tuberculosis cases will be cured by nephrectomy.—*Renal Tuberculosis; its Surgical Treatment, A. G. Hamer, J. Indiana State M. Ass., February, 1921, xiv, 42.*

Tuberculosis of the Anterior Vaginal Wall.—Tuberculous ulceration of the vagina is rarely observed. A case is reported in which the tuberculosis seemed to be limited to the lungs, the head of the cecum and the anterior wall of the vagina. The latter was the only pelvic structure involved in the tuberculous process. There was no evidence of urogenital tuberculosis in the husband. The involvement of the vaginal wall appears to have been hematogenous in origin. It was possible to resect the ulcer with subsequent healing of the lung.—*Tuberculous Ulcer of the Vaginal Wall With Resection of Ulcer, E. K. Cullen, Surg. Gyn. & Obstet., July, 1921, xxxiii, 76.*

Tuberculous Meningitis in Adults.—Tuberculous meningitis in adults presents a very different picture from that in children. The case of a young man of seventeen is reported. He developed symptoms of fatigue, weakness, evening rise of temperature, night sweats and loss of weight, three weeks previous to his entrance to the hospital. Then came lung symptoms, a marked diarrhea and epistaxis one week prior to admission. A diagnosis of typhoid fever was made. Five days before entrance he suddenly developed paralysis of his right hand and inability to speak. This lasted only ten minutes. Physical examination on admission revealed an emaciated young man with a clear mentality, increased pulse and respiration, and fever of 38.4°C. in the morning and 39.8°C. in the evening. There were no other physical findings at that time. Four days later rigidity of the neck developed, and on the following day ptosis of the left upper lid and external strabismus of the left eye. Later there were vomiting, involuntary micturition and defecation, and rightsided hemiplegia. Death ensued in high fever on the fifteenth day from the first nervous symptoms. The principal differences between adult and infantile meningitis are (1) in the former evolution is gradual, (2) the convexity of the brain is involved, and (3) the distribution is in patches. Depending on the location of the patches there may be motor, sensory or psychic symptoms. The motor form may express itself by generalized or Jacksonian convulsions, contractures, monoplegias or hemiplegias, or involvement of the speech centre with resulting aphasia. Headache may be the only symptom and is relieved only by spinal punctures. In the psychic form, delirium, acute mania, melancholic depression or progressive dementia may be present. Comatose and apoplectic forms are also described. Spinal puncture and examination of the fluid are the most important aids. The course in the adult is even more rapid than in the child.—*La meningite tuberculeuse de l'adulte, L Ramond, Progr. Méd., June 11, 1921, xxxvi, 280.*

Pulmonary Tuberculosis, Mycosis and Spirochetosis.—Careful bacteriological examinations would reveal many mycotic and spirochetal infections, which are now diagnosed clinically and treated as tuberculosis, especially in the Southern States. Great emphasis must be placed on this point when dealing with patients coming from the Philippine Islands. A careful examination and observation of pulmonary cases applying for treatment at the charitable institutions in Bangkok, Siam, show that 25 per cent are mycotic or spirochetal. Probably animal inoculation would give an even greater percentage. In an asylum, an examination of 100 patients with symptoms of disease of the lung showed 60 per cent as having spirochetal infection, either pure or associated with tuberculosis or moniliasis. Symptomatically these three conditions are not to be differentiated. Spirochetal and monilial infections may be acute or chronic and there may be every variation between these stages. There is no sign or symptom in pulmonary tuberculosis that may not be simulated by a spirochetal or monilial infection, even to the extreme emaciation and the not infrequent terminal hemoptysis. It has been noted that the character of the sputum in a pure spirochetal infection has a tendency to be watery or mucous, while with a mixed infection it is mucopurulent. Tuberculosis is ruled out absolutely only after animal inoculation. As regards treatment, more may be expected in cases of spirochetosis and moniliasis than in tuberculosis. Arsenic in the first and the iodides in the second condition quite often produce rapid improvement and, not infrequently, perfect cures.—*Pulmonary Tuberculosis, Pulmonary Mycosis and Pulmonary Spirochetosis, R. W. Mendelson, Mil. Surgeon, July, 1921, xlix, 81.*

Atypical Tuberculosis with Mikulicz's Syndrome.—Mikulicz, in 1888 and 1892, called attention to a syndrome of chronic, painless, symmetrical enlargement of the lachrymal and salivary glands, with freedom of the overlying skin from inflammatory reaction. Since then a large number of examples of the affection has been reported. The case here described is unusual in that it presents a typical clinical picture of Mikulicz's syndrome associated with atypical pulmonary and cutaneous lesions. The histological examination of one of the salivary glands and of one of the subcutaneous tumors revealed undoubted miliary tubercles. A search of the literature reveals only three cases of the syndrome which are beyond question tuberculous, and only two other cases with skin manifestations, neither of which resembles this one. The patient, a white American housewife, aged twenty-nine was admitted to the medical clinic of the University of Michigan, June 16, 1920. Her past history was of no interest except for a submucous resection of the nasal septum. This operation was performed in 1913 to relieve itching of the external auditory canal. Before the middle of January, 1920, she had been entirely well. At that time there appeared on each eyelid a swelling which later developed into hard tumors. There was moderate pain during the growth of the tumors which ceased when they attained their maximum size. These were followed by other swellings and tumors in various parts of the body. In April she developed a moderate unproductive cough, accompanied by a slight afternoon fever, the temperature never rising above 99.6°. She had no night sweats, hemoptysis, hoarseness or pleurisy. She was told she had pulmonary tuberculosis, and was sent to the Michigan Tuberculosis Sanatorium. From there she was sent to the University Hospital. Examination showed a poorly nourished woman. In the outer half of each upper eyelid was an irregular, nodular tumor about the size of a large hazel nut, almost cartilaginous in hardness and not tender. There was a general symmetrical enlargement of the salivary glands. The parotids were as large as small eggs and the submaxillary and sublingual glands were as large as hickory nuts. In the lower lip, near its outer ends, were a pair of glands as large as peas, and there was another pair under the tip of the tongue. All were extremely hard, and were entirely without tenderness. Over the upper part of both lungs there were a few persistent fine râles, bronchovesicular breathing and impaired resonance. Other subcutaneous tumors, the size of peas, hard, not tender, and freely movable, were found on the arms and legs. During her stay in the hospital these increased in number, though not in size, until on July 15 it was noted that there were a dozen or more on each arm and leg. They resembled more than anything else multiple fibromata of the skin. Her temperature, pulse and respiratory rates remained normal. The enlarged glands decreased in size except the lachrymal glands which remained in the same condition up to the time of discharge, July 20. Her only treatment had been rest, a high caloric diet and, empirically, syrup of iron iodide. The clinical evidence, combined with the histological examination of the extirpated tumors, put the diagnosis of tuberculosis beyond doubt.—*Atypical Tuberculosis with Mikulicz's Syndrome: Report of a Case, with Unusual Pulmonary and Subcutaneous Lesions, P. L. Marsh, Am. J. M. Sci., May, 1921, clxi, 731.*

Lymphadenoma and Tuberculosis.—Many cases have been described in which tubercle bacilli have been found in the lesions of Hodgkin's disease. The theory is generally accepted that such tuberculosis is secondary. In the case reported no gross tuberculous lesion was found postmortem, the only macroscopic changes being those of Hodgkin's disease of abdominal type. In the affected glands and spleen tubercle bacilli were found in fairly large numbers, for the most part without other cellular reaction than one which appears to be that generally described as peculiar to Hodgkin's disease. It seems possible that in deciding against a connection between the tubercle bacillus and lymphadenoma too much emphasis has been placed on negative results of inoculation experiments. Even if it is admitted that a true lymphadenoma, not caused by the tubercle bacillus, exists, it may well be that the term at present is applied to more than one disease, perhaps including a primary tuberculosis.—*Lymphadenoma and Tuberculosis, I. Fox, Lancet, July 2, 1921, cci, 14.*

Relationship between Graves' Disease and Tuberculosis.—That there is any causal connection between exophthalmic goitre and tuberculosis is most improbable; and when we speak of a relationship between the two affections it must be understood as hypothetical rather than demonstrable. Common to both are tachycardia and fever, emaciation, diarrhea, and vasomotor disturbances, but this syndrome is not peculiar to these two affections. There is also the coincidence of a peculiar eye in each disease, which while by no menas identical has something in common—luminous, moist, etc. Steck, who writes on this subject in the *Schweizerische medizinische Wochenschrift* for June 9, 1921, li, 23, says that when a tuberculous subject has a typical exophthalmus it is of course possible that he has a hyperthyroid component. Poncet indeed pointed out that tuberculous intoxication sometimes causes enlargement of the thyroid, perhaps as a part of a defense reaction. On the other hand, histological studies of many thyroids of tuberculous subjects have failed to show a single case of the alterations which appear in typical Graves' disease. But it has been noted that the thyroid in these cases is never normal—that it may exceptionally be tuberculous but almost invariably is sclerotic. Now, if in a defense reaction developed against tuberculosis the thyroid is disorganized, we can perhaps understand why the pictures of tuberculosis and Graves' disease may largely coincide, and why tuberculosis may be the occasion for a picture of hyperthyroidism of a special type. We say that the tuberculous toxin causes this or that symptom without much effort to explain the mechanism; but if it stimulates the thyroid function we have a ready explanation of some of the symptoms of tuberculosis—tachycardia, low blood pressure, slight fever, the tuberculous eye, and vasomotor phenomena, as the blush on the cheek, part of the tendency to perspire, etc. Such an explanation of early tuberculosis, including so called pretuberculosis, is almost too simple. If true, it would not have escaped the older clinicians. Doubtless it is not difficult to isolate a type of tuberculosis with hyperthyroidism but there is tuberculosis without this component and Graves' disease without any tuberculous factor. The author quotes authorities to prove that in a large material of typical tuberculosis, fully developed Graves' disease is as good as absent. This leaves, then, the association of the bacillary disease with mild and abortive Graves' disease or, as some term it, basedowoid, which is as far as we can go at present without something more than clinical evidence. The author has made use of a method of comparative blood testing which he describes at great length, which seems to demonstrate that the tuberculous subject's blood is quite free from certain substances found in hyperthyroid blood of any degree. The blood of any subject with Graves' disease acts as a synergist to adrenalin in producing vascular contraction, while tuberculous blood is, under all circumstances, quite free from this substance. The petty or minor basedowism of the tuberculous is therefore illusional and due to other factors. The author learned only after he had reached this conclusion that his findings and conclusions were in thorough accord with work recently published by Chvostek.—*Editorial, Med. Rec., August 27, 1921, c, 372.*

Syphilis and Tuberculosis.—The case of a colored man, forty-eight years of age, is reported from the Passavant Hospital of Pittsburgh. A few deep seated nodules on face and neck, which were continuously enlarging, were noticed a year before his entrance. Most of the lesions broke down four weeks later and formed ulcers. These as well as edema of the legs and dyspnea on exertion improved under arsphenamin treatment. The patient had an untreated chancre ten years ago. There was a family history of tuberculosis. On admittance he showed a generalized anasarca, and large undermined ulcerated areas on the lateral surface of the neck, with irregular borders, punched out uneven edges, and profuse discharge. Roentgen ray examination revealed enlarged mediastinal nodes, probably syphilitic. The Wassermann test was positive. A diagnosis of tertiary syphilis and ulcerating gummata was made. Under arsphenamin, iodide and mercury treatment, the patient improved. Three months later he developed ascites. Three litres of turbid fluid were removed. A smear showed 95 per cent of small lymphocytes, no tubercle bacilli, and even injection of the fluid into a guinea pig resulted negatively. The patient died. On autopsy tuberculosis of the peritoneum, intestines, mediastinal and mesenteric nodes, lungs, bronchi and pleura, chronic nephritis and amyloid degeneration of the kidneys, and multiple gummata of the liver and syphilitic aortitis and mitral stenosis were found. The authors believe that the iodide treatment was in part responsible for the patient's loss of resistance and development of miliary tuberculosis. This treatment had been resorted to on account of the marked kidney involvement.—*Tuberculosis and Syphilis, L. Hollander and F. C. Narr, Arch. Dermatol. & Syphilol., August, 1921, iv, 153.*

Influenza and Tuberculosis.—At the Trudeau Sanatorium, a study was made in February, 1919, of the effect of influenza upon tuberculosis. This study included patients in the Sanatorium suffering from influenza and also the discharged cases whose annual reports had been received prior to June 1, 1920. The frequency of tuberculosis following upon an attack of influenza and the reactivation of old pulmonary tuberculosis after influenza was also computed in all cases entering the Sanatorium during the active phase of the epidemic between October, 1918, and December, 1919. In February, 1919, 16 cases of influenza occurred at the Sanatorium. Four of the victims were patients and 12 were nurses, of whom 8 were tuberculous. In no case of their tuberculous patients or nurses was a definite aggravation of their disease found. Of 251 patients in the Sanatorium whose history was carefully gone over for the probable onset of their tuberculosis it was found that 17 had symptoms of tuberculosis antedating their attack of influenza and that 35 had symptoms after the attack. Of the 17 mentioned, pulmonary tuberculosis was proved to have existed before influenza in 14 of the cases, and of the 35 mentioned it was proved after influenza in 26 cases. Reports were received from 2524 discharged patients out of a total of 3055 supposed to be living. Of these, 354 had an attack of supposed influenza and 2160 did not have the disease during the epidemic. Of the former 77 relapsed and of the latter 262 relapsed with their tuberculosis, showing that those having influenza were more subject to relapses of their tuberculosis. Thirty of the 354 cases who had influenza died during the year and 67 of the 2160 who did not have influenza died during the year. It was also found that, as the number of years after discharge increased, the percentage incidence of influenza diminished. Slight rises, followed by a gradual fall, occurred approximately every ten years.—*Influenza and Tuberculosis, F. H. Heise, Thirty-Sixth Annual Medical Report of the Trudeau Sanatorium, 1920, 11.*

Tuberculosis and Arteriosclerosis.—A study of 3578 macroscopic sections at the Pathological Institute at Barmbeck, after excluding all unsatisfactory protocols and all artery changes occasioned by lues, revealed an increased preponderance of fatty deposits (plaques) in tuberculosis over the other cases, with the tendency toward a later and slower development of arteriosclerotic changes; the grade of sclerosis also developing at a later age period. The total male material examined was obtained from 1884 and female from 1502 cases without lues or tuberculosis, and 786 males and 416 females with tuberculosis. Arteriosclerosis was found to arise later in women than in men, and equal grade of involvement was attained only after more advanced years. Fatty plaques had an earlier incidence in women that in men, and were more common among cases of tuberculosis than in the other cases. In spite of the increased incidence of fatty plaques in tuberculosis, definite arteriosclerosis during middle and advanced age was not so common compared with the remaining material. In old age, however, like conditions were found. It is concluded that infectious or toxic agents are causing the fatty plaques and functional disturbances of senile arteriosclerosis.—*Beiträge zur Atherosklerosefrage mit besonderer Berücksichtigung der Beziehungen zwischen Tuberkulose und Atherosklerose, H. Cramer, Virchow's Arch. f. pathol. Anat., March 14, 1921, ccxxx, 46.*

Tuberculous Infection and Delayed Healing.—Two cases are reported with small tuberculous lesions of the eye, which were favorably influenced by treatment with old tuberculin. In the first case operation had been performed for trauma of the eye. Healing was delayed until the ulcers were discovered and treatment given. The second case was one of cyclitis caused by the presence of the lens acting as a foreign body. The lens was removed, but healing did not take place until treatment was instituted.—*Tubercular Infection as a Cause of Delayed Healing in Operations on the Eye, E. B. Miller, Am. J. Ophthal., July, 1921, iv, 516.*

Treatment of Tuberculosis.—The attention of physicians and of the public is called to the ever increasing spread of pharmaceutical and medical quackery in the treatment of tuberculosis. Large numbers of tuberculous individuals are attracted through skilful and unscrupulous advertising to patronize commercialized institutions. The danger of these places is apparent; the patient loses precious time, so that an incipient lesion, still amenable to proper treatment, gradually becomes incurable. The tuberculous patient is drained of his savings, which he would have been able to devote to securing for himself an effective course of treatment in a sanatorium or at a health resort. Also, the isolation of the patient, so necessary to avoid a spread of the infection, is delayed. Many conscientious persons through weakness, courtesy or error of judgment lend themselves to the diffusion of dangerous or unreliable methods. In the hospitals, universities and laboratories, a large number of men are engaged in serious, disinterested research on the value of various drugs, chemical and biological products, sera and vaccines, for the purpose of discovering a cure for tuberculosis. Physicians are urged, while waging a ruthless war on quacks, to be on guard against premature enthusiasm over new remedies. The quest for a specific treatment of tuberculosis is legitimate, but before making any remedy known to the public, before placing it on the market as a new and effective agent, it should be submitted to the most critical examination, in order to afford the necessary guarantee of its value. The remedy should be used in a large number of cases, for a considerable period of time, in order to avoid fallacious coincidences. It should produce, if not constant, at least frequent good results. The efficacy of a method of treating tuberculosis can be gauged only from the progressive and permanent disappearance of the cardinal and objective symptoms of the disease. The patient, who enters any institution for the treatment of tuberculosis, should do so in the hope and belief that he will leave it freed from all signs of active tuberculosis and be no longer a focus of infection. Even in severe cases of tuberculosis cures are achieved much more frequently than the laity believes. The first duty of the physician is to establish the existence of every incipient case by an early diagnosis. It should become a reflex action for the physician to insist upon a sputum examination whenever he is confronted by a patient with a cough. The public must be acquainted with the simple means which are in reach of even the most ignorant to establish for themselves the early diagnosis of this disease. Too much emphasis can not be given to the necessity of placing the public, as well as physicians, on their guard against the prevalent opinion that because a certain remedy is good for one case of pulmonary tuberculosis it must be good for all. This assumption of the existence of a specific cure is bound to prove dangerous, indeed fatal. To treat a tuberculous patient effectively, it is imperative to treat him individually, according to the method most suited to his particular case. It may safely be asserted that once this adaptation of the special remedy to the particular case is fully appreciated by physicians engaged in combating tuberculosis, the treatment of individuals, and consequently of the disease in general, will be productive of excellent results, and will no longer be a vain display, calculated solely to allay the patient's fears.—*The Treatment of Tuberculosis, R. Burnand, Internat. J. Publ. Health, July-August, 1921, ii, 375.*

Institutional Treatment in Surgical Tuberculosis.—This article is a report on the results obtained at the Manchester Residential Schools for Crippled Children over the period of 1905 to 1918. The children admitted must be between the ages of five and sixteen. This may have the result that a number of early cases are missed; as the institution is primarily a school, the type of cases admitted is limited to early noncomplicated cases which have not suffered materially in health. The treatment of the cases has been on conservative lines, with careful and exact fixation. Abscesses are treated by aspiration and very little open operative work is done. Investigation of the after-history of 159 cases, discharged not less than three years ago, showed that of the cases of tuberculous disease of the spine, 34 are alive and well, 10 are alive but with disease still present, and 26 have died. Of the hip cases, 38 are alive and well, 5 alive with the disease still present and 9 have died. Of patients with knee involvement, 28 are alive and well, 1 alive with the disease still present and 2 have died. Six cases with tuberculous disease of the foot are all alive and well. Of the 35 cases who died, 29 showed evidence of abscess formation on admission to the schools. The author believes that the average time needed for the treatment of these cases is longer than has been generally supposed. In his own cases the average duration of in-patient treatment of cases of surgical tuberculosis of the spine and lower extremity is three years and two months.—*Results of Institutional Treatment in Surgical Tuberculosis, E. D. Telford, Brit. M. J., July 2, 1921, no. 3157, p. 8.*

Trudeau Sanatorium Report for 1920.—The number of applicants at the Sanatorium was 459, of whom 355 were admitted. Of the latter, 255 were discharged being classified as follows: In 33, or 12.9 per cent, the disease was apparently arrested; in 108, or 42.4 per cent, the disease remained quiescent; 33, or 12.9 per cent, were improved; 46, or 18.05 per cent, were not improved; in 7, or 2.75 per cent, the diagnosis was doubtful, tuberculosis being suspected; 26, or 10.2 per cent, were found to be nontuberculous; 2, or 0.8 per cent, died. Suspects and the nontuberculous usually remained for a period of less than three months. In addition to the above list, there were treated 50 ex-patients and part time employees, of whom 18 are now at the sanatorium, making the total number of those treated 305. The average term of residence (of those who remained over three months) was five months and eighteen days, ten days longer than in the previous year. One hundred and sixty-one patients gained weight, averaging 11 pounds. Forty-five lost weight, averaging 6 pounds. Forty-six patients had served in the army or navy during the late war, most of whom are being maintained by the Government. In the X-ray department more than 10,000 examinations were made and much valuable research work accomplished. A special study of the early diagnosis of intestinal tuberculosis was made, the result of which is an important aid to the patients at a time when successful treatment can be given. Eighty-one patients have been employed in some capacity during the year, and earned wages approximating $16,500. One hundred and forty-six patients, 19 nurses and 31 ex-patients and others, had instruction in arts and crafts this year. The daily attendance has been 20, a larger average than any previous year. The total time they were occupied was nearly 6,000 hours, and that recorded for the patients 4,939. The working time is prescribed by the physicians. Rattan reed work, jewelry and metal crafts, picture framing and photography were the chief occupations. A few of the ex-service patients attended the Federal Vocational School in Saranac Lake. As a consequence of higher prices, the approximate cost per capita per week was $17.45, or $1.00 more than in 1919. The year 1920 will be remembered for the extravagantly high prices of food, as of all commodities.—*Thirty-Sixth Annual Report of the Trudeau Sanatorium, 1920.*

Rhode Island State Sanatorium Report.—During the year 1920, 497 patients were admitted to the sanatorium and 510 discharged, the whole number of treated patients being 754. Nearly all of the children used the Clear River swimming pool almost daily from May to October with undoubted benefit, local and constitutional. Between April and December, the children received heliotherapy during the daytime by wearing abbreviated trunks so as to expose most of the body. In the restricted sunshine of the winter months, this treatment was intensified in some of the extrapulmonary cases by the use of sun lenses as developed at Porsmeur, France. Thirty-seven cases, having discharging sinuses and tuberculous bones and joints, were treated by violet rays from the mercury quartz lamp. Of 7 cases in which the enlarged lymph nodes disappeared or the sinuses closed, the average duration of treatment was 118 days. Artificial pneumothorax was given to a few selected cases with limited lesion but showing a progressive tendency. Tuberculin was used only in afebrile cases with extrapulmonary lesions. The sanatorium records from 1909 to 1917, inclusive, show that of 121 widowed patients under seventy years of age, 44, or 36 per cent, had been widowed by tuberculosis. This percentage is about three times as great as in the general community. In the fall of 1918, 40 per cent of the adult ambulant patients had influenza. Of 789 tuberculous individuals admitted during 1919 and 1920, in which a full history was obtained, 317, or 40 per cent, claimed to have had influenza since August, 1918, and as 80 per cent of these attacks were dated between September, 1918, and April, 1919, most of them were probably true influenza. Fifteen per cent of the patients admitted during the past two years date the clinical onset of their tuberculosis from an influenzal attack. In only 8 per cent of the patients and employees of the Sanatorium, whose tuberculous disease was quiescent or better, was there a relapse of tuberculosis activity after influenza. The number of applicants for admission in the year following the epidemic was not increased. A sanatorium problem resulting from the influenza epidemic which will persist a long time is the number of cases of chronic bronchitis, bronchiectasis, unresolved pneumonia, and abscess of the lung, heretofore rare but now comparatively frequent, which come to the sanatorium and the diagnosis of which requires careful study. Of the 479 patients admitted during the past year, 379 were on the free list and many patients were transferred to the free list after admission, so that of the 87,351 days' treatment, 74,049, or 84 per cent, have been made free. The weekly per capita cost of Sanatorium treatment for 1920 was $16.99, which was an increase of more than 23 per cent over that of the previous year. This great inflation of prices in 1920 was unexpected and resulted in a deficit of $14,637.13. During the past year 25 ex-service men were cared for. A special sale of patients' handicraft articles netted over $400. The equipment for light therapy has been increased by the purchase of a mercury quartz lamp and by the donation of two sun lenses. The sanatorium should be safeguarded by chlorination of the water supply from Wallum Lake.—*Sixteenth Annual Report of the Rhode Island State Sanatorium at Wallum Lake, 1920.*

Vaccination Against Tuberculosis.—Tuberculous infections can be prevented only by vaccination. Biological tests are necessary in the truly early stage of tuberculosis, to establish a positive diagnosis of the presence of tubercle in the organism. In an analysis of reactions of 1,315 individuals, no reaction of any kind was noted in 25, or 1.7 per cent; local reactions occurred in only 366, or 28.3 per cent; and general febrile, or focal reactions, were observed in 924, or 70 per cent. Therefore no infection had occurred in 1.7 per cent, there were no tuberculous lesions accessible to the circulation in 28.3 per cent, and 70 per cent were actually tuberculous and liable to further progressive disease. Including previously vaccinated cases with the above, and adding vaccinations made since, 3000 children have been vaccinated since 1903. Apart from the biological tests of the blood and the general and local improvement which followed promptly, not a single case is known to the authors in which the tuberculosis recurred or became active. The time, however, intervening since their vaccination is entirely too short to form final conclusions. Unless vaccination is resorted to in the first years of life, the infection as a rule is already accomplished. Children in a tuberculous environment should be vaccinated immediately or soon after birth. There should really be no selection of cases. Every child should be vaccinated, although the administration of the vaccine should be deferred in instances where other diseases are present, especially where the symptoms thereof would interfere with the observations of reactions, as, for instance, fever or acute catarrhal affections of the air passages. There is no reason for delay. The earlier the child is vaccinated, the better is the prospect that no infection with tubercle bacilli has occurred. The authors are frequently asked in what respect their vaccine differs from the various tuberculins and from the tubercle bacillus emulsions in the market. They answer that it contains only the albumoses, albumins, nucleoalbumins, fatty substances, and lipoids of tubercle bacilli in proper proportion, obtained without subjecting them to physical or chemical injury, and represents all organic body substances of the tubercle bacillus in solution. Tuberculins as first made by Koch, and thereafter by others, are derived from the liquid media upon which tubercle bacilli have been grown and have thereafter been filtered out; they contain little or no bacterial body substance. Emulsions simply represent the tubercle bacilli after having been separated by shaking or grinding of the bacilliary mass, the emulsion being sterilized by heat. The authors' studies show that in 28.3 per cent of their cases infection was overcome, or the lesions had become obsolete. This proves that tuberculous lesions still accessible to the circulation can be made to disappear by the use of specific vaccines. The rapidity and the uniformity of the results of vaccination depend upon the time elapsed from the inception of the infection, the extent which the lesions have reached, and the degenerative alterations present.—*Vaccination Against Tuberculosis, K. von Ruck and R. E. Flack, Med. Rec., June 18, 1921, xcix, 1048.*

Treatment of Tuberculous Adenitis.—Tuberculous lymph nodes may be simply hypertrophic or in addition there may be sclerosis or caseation. The nodes may be hard to palpation and yet have begun to caseate in the centre. The medical and hygienic treatment consists of substantial food and fresh air and a sojourn at the seaside, if possible. The latter must be sufficiently long, as otherwise recurrences are likely to occur. Codliver oil and Fowler's solution are also important aids to local treatment. The latter may be physical or surgical. The physical agents are radiotherapy, which is especially favorable in the simple hypertrophic form and heliotherapy which gives excellent results in fistulous forms with secondary infection. In the nonsuppurating forms, interstitial injections of ether and iodoform, glycerin and iodoform, or iodoform and creosote may be given, with the object of producing sclerosis. When it is desired to obtain softening and suppuration, camphorated thymol is of use. After this result is obtained, the treatment, as in all suppurating forms, is aspiration, care being taken to aspirate at a point in the periphery of the abscess and parallel to its wall. This may be followed by the injection of 10 per cent iodoform in ether. Extirpation is sometimes indicated in adherent and fistulous processes which have resisted all other treatment.—*Traitement des adénites tuberculeuses, A. Broca, Progr. Méd., May 21, 1921, no. 21, 227.*

Treatment of Tuberculous Adenitis by Roentgen Rays and Radium.—In the treatment of tuberculous adenitis better results are obtained from the use of radium and the roentgen rays than by any other method. Radiotherapy alone will cure over 90 per cent of the cases. At present, surgeons of experience are not operating primarily for tuberculous adenitis. If they operate it is only to remove fibrous nodes after the tuberculous foci have been destroyed by roentgen rays or radium. These hard, fibrous nodules seldom ever contain tuberculous foci, but it may be advisable to remove them as one would a foreign body, through a small incision. Experience has proved that tuberculous adenitis is not primarily a surgical disease. Many laryngologists will not remove diseased tonsils if the cervical nodes are enlarged until the nodes have been given a thorough course of treatment, either by roentgen rays or radium. Radiation of the enlarged cervical nodes is important before removing the tonsils of children under fifteen years of age, and particularly so if under the age of five or six, as the lymphatic vessels are wide open, and in the removal of the tonsils before radiation there is danger of producing a general infection if tuberculosis is present. In the treatment of tuberculous adenitis the most important thing to be remembered is that it is a local manifestation of a constitutional disease. Prophylactic treatment should be given more attention, and an effort should always be made to find the channels of infection. The importance of removing unhealthy tonsils, bad teeth, etc., should not be overlooked. Since the disease can be removed successfully by roentgen rays or radium, complete extirpation of the tuberculous nodes should never be performed until the disease is well localized. When the old methods of treatment are employed a certain percentage of the patients acquire pulmonary tuberculosis. This possibility never occurs when radiation is given before any lung involvement takes place. For this reason, medical treatment should not be persisted in too long without radiotherapy. Large nodes due to an inflammatory process are frequently secondary to a septic condition elsewhere and a search should be made for the primary lesion. When this is found and treated, if the nodes remain large, and particularly if they show a tendency to suppurate, radiotherapy should be employed at once. Suppuration can nearly always be avoided when this treatment is given properly and promptly. Constitutional infection is not uncommon when tuberculous nodes are neglected. As long as the nodes do not suppurate they are usually checking the tubercle bacilli but they are undergoing pathological changes. Untreated tuberculosis of the nodes is often followed by tuberculosis of the bones and joints, and finally there is an extension into the lungs. In the treatment of tuberculous adenitis in the future, when a more systematic raying is employed and when the cases are referred earlier, this method of treatment will be universally accepted.—*The Treatment of Tuberculous Adenitis by Roentgen Rays and Radium, R. H. Boggs, Am. J. M. Sci., July, 1921, clxii, 90.*

Severing Adhesions Impeding Therapeutic Pneumothorax.—Jacobaeus describes his experience with cauterization of bands and other adhesions in 40 cases of pulmonary tuberculosis in which artificial pneumothorax was indicated. There was never any serious hemorrhage in any instance from the cauterization, and only once loss of 100 or 200 cc. of blood. Pleural exudation followed, however, in 50 per cent. The exudate was absorbed in a week or two in most of the cases, but in 8 per cent it progressed to a serious tuberculous empyema which proved fatal in three of the cases. In 75 per cent of the total 40 cases the desired result was attained by breaking up the adhesions with the actual cautery, thus enabling effectual compression of the lung by the pneumothorax, which otherwise would have been impossible. A number of instructive roentgenograms are reproduced. Jacobaeus first proclaimed the feasibility and the advantages of the procedure in 1913, and now, besides his own forty cases, Holmboe, Skärgard, Saugman and others have applied this method with gratifying results. The thoracoscope is introduced through a cannula, and an outline sketch of the bands seen is drawn to serve as a map. With this as a guide, the actual cautery is introduced through the cannula and the adhesions severed.—*The Cauterization of Adhesions in Pneumothorax Treatment of Tuberculosis, H. C. Jacobaeus, Acta Chirurg. Scandin., March 7, 1921, liii, 293.*

Artificial Pneumothorax.—Pneumothorax treatment is indicated every time that life is threatened by the extension of the local lesion, according to Forlanini. The condition of the other lung must be investigated by the X-ray. Care is recommended in diagnosing disease in the better lung from sounds which are merely conducted. Sharp consonating crepitations are nearly always audible on the opposite side near the spine and about the axilla, though they may be less plainly heard in some cases in the area between these points. Often a pneumothorax will unexpectedly remove signs in the functionating lung. It is not wise to let refills run above 700 or 800 cc. and in most cases 500 cc. or even less is a preferable amount. The interval depends on the quantity and on the rate of absorption. A long interval may allow of expansion and attachment of an imperfectly collapsed lung. Mediastinal overdisplacement may be difficult to discover without X-ray examination. The symptoms may be vague and the position of the heart may not appear to be unduly altered. Increase of pressure because of the onset of pleurisy is not a rational procedure. Surgical treatment of adhesions and extrapleural thoracoplasty are difficult but attended with success in skilful hands.—*Artificial Pneumothorax, C. Riviere, Brit. M. J. June 4, 1921, no. 3153, 810.*

Artificial Pneumothorax in Treatment of Hemoptysis.—In 10 of the 11 cases the hemoptysis was merely an additional indication for the collapse therapy of the unilateral destructive tuberculous process. The tendency to hemorrhage from the lungs was arrested at once, and it never returned in the 6 cases of complete pneumothorax. In the others, further measures to compress the lung were required later. In an eleventh case it proved impossible to induce the pneumothorax, and death ensued from pneumonia. Necropsy revealed that the bleeding had been from the supposedly sound lung, although nothing had suggested this during life; not even roentgenoscopy. No roentgenogram had been made.—*Haemoptyser behandlede med Pneumothorax Artificialis, J. Begtrup-Hansen, Ugesk. f. Laeger, March 31, 1921, lxxxiii, 457.*

Nonoperative Treatment of Surgical Tuberculosis.—Surgery still plays a part in the treatment of bone, joint and lymph node tubercle, though in cases of active disease it is continually diminishing. Conservative treatment is defined as the adoption of all measures which tend to improve the patient's general health, increase his powers of resistance, and preserve or restore the part or parts attacked, while radical treatment aims at the cure of the disease by the removal of the local lesion. Conservative treatment also includes the education, instruction, manual training and amusement of the children, and the prevention of tuberculosis in those exposed to the disease. Concerning local treatment the rule is stated that tuberculous abscesses, secondary to disease of the spine, hip or any of the larger bones or joints, should never be opened. They should be aspirated as soon as possible after their formation. Important adjuvant methods are heliotherapy, balneotherapy, chemotheraphy, vaccine and X-ray treatment. Attention to teeth, skin, throat, nose, ears, and eyes must not be neglected. A department for the after-care of these patients is of the greatest importance. Tables and illustrations representing the good results obtained at the Lord Mayor Treloar Crippled Hospital at Alton, England, are included in this report.—*The Nonoperative Treatment of Surgical Tuberculosis, H. Gauvain, Lancet, May 21, 1921, cc, 1065.*

Chaulmoogra Oil in Leprosy and Tuberculosis.—A recent experimental investigation has been made with derivatives of chaulmoogra oil, especially sodium morrhuate, sodium gynocardate and hydnocarpic acid, which had proved effective in the treatment of leprosy, in animals infected with tuberculosis. In the acute general tuberculosis produced in very susceptible animals, the results were entirely negative, except for an early febrile reaction followed by a fall of temperature, in 2 goats which eventually succumbed to the infection at about the same time as a control animal. It is pointed out that these animal infections are equivalent to acute general tuberculosis in man, so that the failure in such cases does not prove the drugs to be useless in the more chronic forms of tuberculosis, which form the great majority of human cases. Rogers concludes that these drugs are worthy of further trial in the more chronic forms of the disease, and especially in lupus and surgical tuberculosis, where any changes will be visible and easily observed.—*Chaulmoogra Oil in Leprosy and Tuberculosis, L. Rogers, Lancet, June 4, 1921, cc, 1178.*

No Compromise with Bovine Tuberculosis.—Reports state that tuberculosis is prevalent in from 40 to 80 per cent of all livestock in Germany and other foreign countries. In certain thickly populated cattle districts of America, bovine tuberculosis exists in from 25 to 30 per cent. In view of these figures it is difficult to understand articles appearing, not infrequently, in various veterinary publications, farm journals, and livestock papers criticizing the work being done by associations to establish methods and rules for tuberculosis free accredited herds. The chief objection voiced by these writers seems to be based on what they consider the indiscriminate slaughter of reacting cattle. In 1917, an organization for coöperative tuberculosis eradication was effected in the United States between the Bureau of Animal Industry, the livestock sanitary officials of the various States and the livestock owners. The policy of this campaign is that an animal which has once been classed as tuberculous is and should remain definitely marked as a potential danger to healthy cattle with which it might come in contact. The records of the Bureau show that from April, 1920, to the end of March, 1921, approximately 92 per cent of the reactors slaughtered were found to be diseased. Many additional cases were disclosed by laboratory examination of suspected lymph nodes and by animal inoculation. Reports for the last few months indicate that an average of over 125,000 head are being subjected to tests monthly. This alone would prove the satisfaction with which the work has been received by the most interested parties, namely, the livestock owners themselves. Other criticisms are (1) abattoir statistics on the slaughter of calves indicate that calves under six months of age are less susceptible to infection than adult cattle, and (2) one exposure to infection is possibly not a serious matter. Since the intracutaneous method of testing has become generally used, it has been proved that in areas in which a considerable amount of infection has been found a large percentage of calves originating in such herds will react either as calves or at a later date. The thought that one exposure to infection of tuberculosis is to be lightly regarded is pernicious. Any measures which give the benefit of the doubt to tuberculous animals redound only to the discredit of the profession. Fully 90 per cent of livestock owners who had the opportunity of holding valuable cattle in quarantine for breeding purposes, have refused such offers. In handling such an insidious disease as tuberculosis, the idea of holding infected cattle is repellent to livestock owners.—*No Compromise with Bovine Tuberculosis, L. B. Ernest, J. Am. Vet. M. Ass., August, 1921, lix, 603.*

Accredited Herd Plan and the Practitioner.—An accredited herd is one in which no animal affected with tuberculosis has been found by physical examination upon two annual or three semiannual tuberculin tests, applied by a veterinary inspector of the United States Bureau of Animal Industry, or a regularly employed veterinary inspector of the State. The detection of tuberculosis depends almost entirely upon the use of tuberculin tests. The initial testing in accredited herd work may be performed by the subcutaneous or intracutaneous method. The ophthalmic method may be used only in combination with the subcutaneous or intracutaneous test. The subcutaneous, until recently, has been the only officially recognized and generally used tuberculin test. The ophthalmic method now ranks very high. The Bureau of Animal Industry for some months past has supplied inspectors with tuberculin discs for conjunctival use. Each disc contains 0.1 gm. O. T. Only one eye is treated, the other eye being observed as a control. The first tablet is used as a sensitizing agent, and the second is referred to as the diagnostic tablet. Occasionally, in the case of an uncertain reaction, a third tablet should be applied about four or five hours following the second disc. The best results are obtained when the tablet is inserted well up under the upper eyelid, where it lies contiguous to the secreting structures, the lids being held in apposition until the tablet has dissolved, which will be about thirty or forty seconds. There seems to have been no official code adopted for the reporting of ophthalmic reactions. The author suggests the folowing: x = the amount of mucopurulent exudation; l = lacrimation; h = hyperemia; sx = slight exudation (2 to 4 minims); mx = marked exudation (5 to 10 minims); ex = extensive exudation (more than 10 minims). All animals exhibiting less than sx would be classed as suspicious, and those presenting sx or more would be classed as reactors. The control eye should remain normal. If after insertion of the diagnostic tablet observations have been made every two hours until the twelfth or fifteenth and no reaction is evident, the animal may be classed as apparently free from tuberculosis. The Bureau supplies an especially prepared intracutaneous tuberculin, containing 50 per cent of concentrated O. T. From 0.1 to 0.2 cc. of this tuberculin is injected by means of 2 cc. syringe with a curved or straight 24 gauge needle, or a Schimmel dental needle may be used. The site of injection is in either of the subcaudal folds or in the immediate vicinity, where the skin is soft and pliable. The veterinarian must realize the importance of feeling the condition of the subcaudal folds at the time of injection. If he knows the normal feeling he will recognize the abnormal feeling. This is an essential point in the determination of a reactor. If any abnormality of the skin under the tail is observed, the character of the condition is to be noted, with the identity of the animal. Then when a reaction appears, the animal must be eliminated from the herd. Instructions have been or soon will be issued by the Bureau of Animal Industry with reference to the examination for recognition by the State and Federal authorities as qualified veterinarians for the tuberculin testing of accredited herds, and the places at which it will be held. The State and Bureau solicit the interest and hearty coöperation of every qualified veterinarian.—*The Accredited Herd Plan, the Tuberculin Tests, and Their Relation to the Practitioner, W. C. Dendinger, J. Am. Vet. M. Ass., August, 1921, lix, 615.*

Bovine and Human Tuberculosis.—In the crusade which is now being waged against tuberculosis the veterinarian must be vigilant and do his part in insisting upon elimination from dairy herds of all tuberculin reacting animals. Unfortunately, the owner of the reacting animal often takes a purely economic view of the matter. This attitude, backed by the apathy of the milk consuming public, serves to handicap materially the work along these lines. Cows reacting to the unofficial test though in a good physical condition are not infrequently left in the milking herd or, if eliminated, take their place in the herd of a neighbor, or in the herd of a distant State whose borders they cross in spite of laws to the contrary. Their presence there then establishes new foci of tuberculosis from which the disease may be spread far and near. According to figures compiled by Park, of the New York City Board of Health, the frequency of bovine tuberculosis in man as collected by various investigators is as follows: In adults, 955 cases have been examined of which 940 showed human infection and 15 bovine infection. In children from five to sixteen years of age, out of 177 cases investigated, 131 were human and 46 bovine infections. Among children under five years of age there were 368 cases, of which 292 were found infected with the human and 76 with the bovine type. Park also cites 9 cases under six years of age, who were fed exclusively on cow's milk at the Foundlings' Hospital. Five of these children died of bovine and 4 of human infection. At the Babies' Hospital where the infants are nursed or fed on prescription milk, out of 63 children dying of tuberculosis, 59 proved to be human and 4 bovine infections. In England, 23 to 25 per cent of the fatal cases of tuberculosis in children are due to bovine infections. Stiles, of Edinburgh, reports on 72 cases of tuberculous cervical lymph nodes operated on at the Children's Hospital, in which the disease was due to the bovine bacillus in 65 cases and in only 7 to the human. It must be understood that the cow with a tuberculous udder is not the only source of danger. The cow with an open tuberculous lesion which is eliminating the bacilli with the expired air in the acts of bellowing and coughing, or with the feces, the urine or vaginal discharges, contaminates herself, the neighboring animals, and her stable. From these sources the bacilli may get into the milk at the time of milking or subsequently. It must be remembered also that it is not only the visibly affected cow that may eliminate tubercle bacilli in her milk and that this elimination may not be constant. A bacteriological examination of the milk of a reacting cow, if negative, is not conclusive evidence that the milk of the animal is harmless so far as tuberculosis is concerned. In Georgia, dairy herds are free from tuberculosis, due to the fact that they are more or less isolated and comparatively few in number; also there is little interstate traffic of dairy animals. That such an ideal condition shall continue, the veterinarians of the State must be ever on guard against the introduction of this devastating disease.—*The Relation of Bovine to Human Tuberculosis and the Status of the Veterinarian in the Fight to Control This Disease, A. G. G. Richardson, J. Am. Vet. M. Ass., August, 1921, lix, 609.*

Skin Tuberculosis in Cattle.—This disease in cattle, when due to the bovine bacillus, appears for the most part in the verrucous form. The lesions are circumscribed, and in close proximity to the skin. Unless a careful search is made they may be overlooked. They have a tendency to locate in distal parts, particularly in the extremities where the circulation is limited. They are more prevalent below the knee or hock, although they may be scattered over the body along the course of the lymph nodes. Generally they are calcareous or caseocalcareous, slightly hardened and irregular in outline, and vary in size from a small pea to a walnut. Occasionally they are hard or horny and may be covered with a crust. The overlying skin is frequently thickened. In color the lesions are grayish yellow or light pale yellow. An unhealed lesion may be present, but ordinarily the skin presents no unhealed surfaces, especially if the disease has been present for any length of time. As tuberculosis cutis is practically a painless affection, any history is usually lacking, but the disease is much more prevalent than is generally supposed. Healthy cattle, quartered in yards with cattle affected with visceral lesions, become inoculated through lying on the excreta of the infected animals. This is particularly true in the West where the cattle occupy a common feed yard with other livestock, and manure is removed at uncertain intervals. Examination of cattle for tuberculous skin lesions could be made advantageously whenever tuberculosis is indicated or suspected as a result of the tuberculin test. Careful palpation of the skin, especially in the region of the extremities, should be made and any suspected thickness or other abnormalities noted. If this record accompanied the animal when submitted for slaughter, it would aid the postmortem examination. The latter should include a careful palpation of the skin of the extremities. It is an easy matter for a small tuberculosis lesion, the size of a millet seed or pea, to be removed or destroyed during the rapid method of removing the hide so often practiced in establishments having a large volume of slaughtering operations. For this reason the removal of the feet should be permitted only under the direct supervision of the attending veterinarian.—*Tuberculosis Cutis, W. D. Wright, J. Am. Vet., M. Ass., August, 1921, lix, 598.*

THE

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ABSTRACTS OF TUBERCULOSIS

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The Abstract Editor is Dr. George Mannheimer, 41 West 51st Street, New York City. Prompt transmission to him of reprints or abstracts of papers on tuberculosis, sanatorium or board of health reports, etc., will promote their early publication in this section.

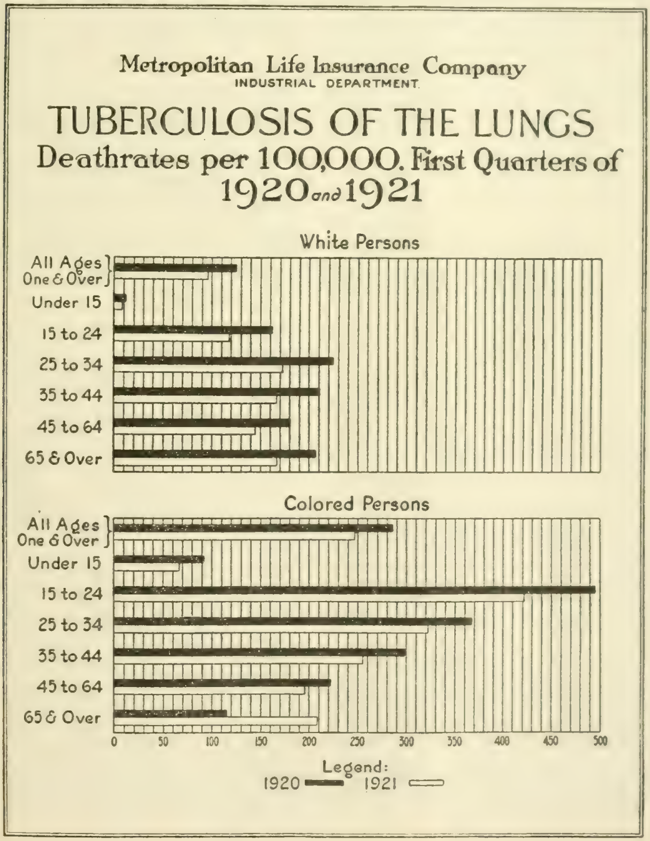
Abstracts should be sent typewritten on one side of the page only. They should be as concise and compact as the subject matter of the article warrants. They should be headed with a short title, and followed by the full title of the paper, author's name, journal, date, volume and page.

Mortality and Morbidity from Tuberculosis in the United States.—In 1917, nearly three-fourths of the total population of the United States were within the Registration Area. The tuberculosis death rate per 100,000 in this area was 146.3. The intensive survey by the Framingham Community Health and Tuberculosis Demonstration, special investigations of tuberculosis associations, the records of insurance companies, and the physical examination of men drafted into the military service, lead to the conclusion that there are 7 active cases of tuberculosis for every death in a given year. This would amount to about 1,000,000 cases, or 1 per cent of the population. There also are probably at least 1,000,000 more inactive, arrested or latent cases. The mortality rate has steadily decreased, but whether the morbidity has increased or is only apparent because of rapid advances in general knowledge of tuberculosis and its more frequent and accurate recognition, is open to debate. The trend of the campaign against tuberculosis in the United States is more toward building up the resistant powers of the individual, although emphasis is laid on the prevention of infection. The necessity of protecting young children from massive infections is fully recognized, but conquering tuberculosis by separation, segregation and fumigation has lost popularity. The development of antituberculosis work and of the scientific methods of clinical diagnosis of bacillary infection are based upon the clear distinction between tuberculous infection and tuberculous disease. The general practitioner is urged to examine the sputum of his own cases rather than to depend upon the public laboratories where pressure of time leads to carelessness in the study of smears. Many specimens containing tubercle bacilli may be reported negative. Fifteen minutes at least should be spent upon every specimen before concluding that bacilli are absent. The roentgen examination of the lungs should be used more often than is at present being done, as a supplement to the physical examination of the chest. It should never be used as the sole means of diagnosis. Complete anamnesis is the most important means of determining the presence of clinical tuberculosis. The general practitioner must be taught to hear, recognize and properly interpret important adventitious sounds, particularly the recognition of râles, their localization and persistence, the elimination of spurious râles, and the significance of breath and voice sounds. He must understand the essentials of percussion, and recognize asymmetries, delay of respiratory movement and limitations of expansion. A wider use of the microscope for personal examination of the sputum is deemed of extreme importance. Attention is called to a post-graduate course given in July and August of each year for the study of tuberculosis by the Trudeau Foundation at Saranac Lake. Usually there are more than twice as many applicants as can be admitted. To help meet this demand, 16 physicians of Colorado Springs have organized the Colorado School of Tuberculosis. The schedule is similar to that of the Trudeau School and the course is likewise limited to 25 students. Plans are being laid for the inauguration of similar courses at Asheville and Los Angeles. The recent development in the United States of medical field consultation services is a distinct forward step in the graduate instruction of physicians.—*Mortality and Morbidity from Tuberculosis in the United States of America, with an Outline of the Development of Scientific Methods of Clinical Diagnosis of Bacillary Infection, H. A. Pattison, Confér. internat. contre la tuberc., October 17–21, 1920, 89.*

Control and Treatment of Tuberculosis in Great Britain.—In England, up to September, 1920, the Ministry of Health (established in June, 1919) and their governmental predecessors had approved 422 tuberculosis dispensaries, and in Scotland 24 had been similarly approved. For the same period in England, 97 sanatoria had been approved and cases of tuberculosis received by 93 infectious disease hospitals and infirmaries. The number of beds totaled 15,781. In Scotland during the same period, 21 sanatoria had been approved and 59 infectious disease hospitals and infirmaries received tuberculosis cases. The number of beds totaled 2,997. A number of local authorities have instituted working colonies as part of the tuberculosis scheme. Recently, especially in connection with discharged service men, the Government has had under consideration the establishment of one or more village settlements, which would provide accommodations for the residence and occupation of tuberculous persons whose health is seriously, perhaps permanently, impaired. Administration service since June, 1919, has been under the Ministry of Health in England, and under the Board of Health in Scotland. In 1914, notification of all forms of tuberculosis was made compulsory throughout the Kingdom. The Government has undertaken to contribute toward the cost of institutions for the treatment of tuberculosis at the rate of 180 £. per approved bed. Towards the maintenance of approved institutions, the Government has undertaken to contribute 50 per cent of approved expenditure.—*The Control and Treatment of Tuberculosis in Great Britain, R. Philip, Confér. internat. contre la tuberc., October, 17–21, 1920, 151.*

Prevention of Tuberculosis in the United States.—In the United States the organization for the prevention of tuberculosis consists of two great forces: 1. Governmental or regular force commanded by State Tuberculosis Commissions, by Tuberculosis Departments of State Boards of Health, and by the surgeon-generals of the Army and Navy and Public Health Service, and composed of thousands of doctors and nurses who founded and conduct tuberculosis sanatoria and dispensaries and clinics; and of other thousands of tuberculosis nurses who seek out patients and attend them and separate them from their endangered families. This governmental force secures also the enaction of necessary legislation concerning the safeguarding of the public from tuberculous meat and milk, and concerning the securing of such housing and street regulations as will assist in the prevention of the disease. 2. A volunteer force of which the central council is the National Tuberculosis Association. The functions of this Association are chiefly advisory, but as its membership consists of practically all the prominent physicians and social workers interested actively in the crusade against tuberculosis, its advice has had usually the effect of a command, and is followed in all parts of the country, even by those who sometimes doubt the wisdom of a given pronouncement. In America, as in other countries, the tuberculosis death rate increased during the war, and dropped decisively after the war. The explanation of this is not as yet forthcoming. A part of the American organization for the prevention of tuberculosis which calls for particular attention is the Framingham Health and Tuberculosis Demonstration. It is too soon to give results, but the Demonstration has taught that preventable and curable disease in children is in much greater proportion in every community than was expected, that the general practitioner utterly fails to diagnose tuberculosis, and that at least ten active clinical cases of tuberculosis are to be found for every death from tuberculosis in the community. It has taught the necessity of having expert advice to assist the ordinary family doctor.—*The Organization for the Prevention of Tuberculosis in the United States of America, S. J. Maher, Confér. internat. contre la tuberc., October 17–21, 1920, 170.*

Tuberculosis Death Rate Still Declining.—The death rate for tuberculosis of the lungs was 20.7 per cent lower in the first three months of 1921 than in the corresponding period of 1920. There was a greater decline among white persons (23 per cent) than among colored persons (14 per cent). The group of insured white persons under 25 years of age shows a reduction of 27 per cent in the mortality from this disease. A 26 per cent reduction is observed for colored persons under 15 years of age and of 15 per cent between 15 and 24 years. With advancing age, there is a tendency toward reduction in the percentage of decline in mortality for both white and colored lives. If the present downward tendency of the tuberculosis death rate continues, 1921 will have a mortality figure for this disease surpassing the records of all previous years in the public health history of the United States. The most encouraging feature of the current tuberculosis mortality record is that great declines are occurring at those ages where the rates are highest. The appended chart illustrates the facts.—*Statistical Bulletin, Metropolitan Life Insurance Co., July, 1921, ii, No. 7, 3.*



The Control of Tuberculosis.—The science of heredity of human diseases is still in its infancy. If hereafter it can be demonstrated that tuberculosis is influenced by hereditary factors, direct attack on environmental factors will remain the chief method of public control of the disease. The known measures for the control of tuberculosis, in addition to the success they may achieve in its prevention, will improve the conditions of life and work of the entire population, and will assuage the suffering and ameliorate the lot of tuberculous patients. In tuberculosis there is no reason to doubt that, when public authorities are prepared to take the completely practicable steps for guiding the life of every known consumptive patient in the population, a rapid reduction in this disease can be secured, and that in one or two generations the death rate from tuberculosis might be reduced to one-half of its present amount.—*Some Considerations on Tuberculosis, A. Newsholme, Brit. J. Tuberc., July, 1921, xv, 105.*

The Real Problem of Tuberculosis.—The greatest problem in the treatment of tuberculosis to-day is not the discovery of a specific therapeutic agent, but it consists in the establishment, among people in general, of a proper mental attitude toward the disease. Because of statistics like Naegeli's, showing the presence at autopsy of apical scars in the vast majority of lungs, because of the widespread prevalence of positive Pirquet reaction, because of Liebermeister's demonstration of tubercle bacilli in the circulation in the early stages of the disease, and because of the oft repeated demonstration of living tubercle bacilli in the lymph nodes of supposedly non-tuberculous children, Saathoff is inclined to believe that among civilized races tuberculous infection is universal. If the patient with clinical disease can be made to see that all his fellowmen are engaged in the same battle as himself, and that most human beings come off victors, phthisiophobia will no longer exist, and a most helpful mental attitude will be established.—*Das Kernproblem der Tuberkulosebekampfung, L. Saathoff, Münch. med. Wchnschr., July 8, 1921, lxviii, 842.*

The Framingham Experiment.—The plan of the Framingham Demonstration is described in detail for the benefit of French readers. The results obtained in 1917–1918 are classified and set out under conspicuous headlines. The account is appreciative and optimistic.—*L' experience de Framingham. Un chapitre de is la lutte anti-tuberculeuse aux États-Unis, A. Raphael, Rev. d. l. tuberc., 1921, ii, 129.*

By-Products of the Tuberculosis Movement.—Tuberculosis has played the part of a stern, chastising schoolmaster in teaching the people the subtle virulence of germs of disease which could neither be seen nor handled. During the war much was learned about glanders and the marvellous results of mallein vaccines. The lesson to be taught now is that results in the eradication of tuberculosis cannot be brought about immediately. The third lesson is that to understand the laws of the disease, coördination with work in other and allied fields of pathology is necessary. The diseases of man are to be studied side by side with the diseases of plants and animals. The physician and his veterinary colleague must work as partners. During every moment of our lives we are dependent for good and evil upon unicellular plants. Principles cannot be parcelled out between the several aspects and departments of medicine. Constant mutual enlightenment on systematic lines between physicians and veterinarians is essential if the two schools are to comprehend each others' work. Evolution is one of the keys to pathology as it is to biology. Until institutes of comparative pathology are established, the science and art of medicine will lag on the way.—*Beneficent By-Products of the Tuberculosis Movement, T. C. Allbutt, Brit. J. Tuberc., July, 1921, xv, 101.*

Medical Education in Tuberculosis.—Tuberculosis is a disease which has to be taken into consideration in the differential diagnosis of almost every other disease. It is capable of affecting every organ of the body. The most opportune time, then, for acquiring a comprehensive and special knowledge of tuberculosis is after graduation. Now that there are so many wholetime appointments in connection with tuberculosis, it is probable that the provision of special courses of instruction would meet a definite want and that opportunities for advanced study would be welcomed by a considerable number of medical men. In this connection, the granting of a Diploma of Tuberculosis is to be desired, as it would add an inducement for special study, ensure a general improvement of the standard of applicants for wholetime employment and give to those charged with selection for such posts a guarantee that the candidates have devoted time and attention to their subject. Assuming that the regulations governing the granting of diplomas or certificates will exact standards of age, experience, and professional standing, at least equal to those claimed as desirable for tuberculosis physicians in the Interim Report of the Departmental Committee on Tuberculosis (1912), the men that present themselves for training will be already well equipped as regards the details of routine clinical diagnosis and treatment. For these men to get the best out of a course of training in tuberculosis the teaching should be concentrated on principles rather than on details. The students must be prepared to take a wide and intelligent view of the subject to which they propose to devote their careers. They must be shown that the ward, the laboratory, and the statistical bureau are complementary to one another, not separate or antagonistic, and be inspired with an enthusiastic curiosity that will lead them on to lives of observation and research.—*Training in Tuberculosis, S. L. Cummins, Brit. J. Tuberc., July, 1921, xv, 109.*

The First Sanatorium.—Symes Tompson, in his article appearing in the *Practitioner*, June, 1921, states that the credit for starting the first sanatorium belongs to Hermann Brehmer who opened an institution at Görbersdorf in the Waldenberg Mountains in 1859. Mention is made of George Bodington's paper published in 1830, but no mention is made of the fact that Bodington started an establishment for the reception and treatment of consumptives prior to this date in the village of Sutton Coldfield; but so hostile was the medical profession then to the method of treatment that he gave up the curing of consumption and transformed his hospital into a lunatic asylum.—*The History of Tuberculosis, E. Cureton, Practitioner, August, 1921, cvii, 145.*

The Future of the Sanatorium.—The main function of a sanatorium is treatment of patients. Except in acute and advanced cases, the general condition of most patients suffering from pulmonary tuberculosis responds quickly to sanatorium regimen. Unfortunately, these patients remain too short a time. Feeling so much better, and fit to resume work, they leave while the lung lesion is often only commencing to heal. Under home and working conditions the tuberculous trouble in the lung is apt to become active again and the patient grows rapidly worse. A longer period of treatment at the sanatorium should be made compulsory and this further treatment should be on the colony plan. The sanatorium and colony should be combined in the same institution. In the colony the patients could, as far as possible, continue their usual occupations. The sanatorium would then become the centre of a tuberculosis community. In the sanatorium of the future there should also be greater facilities for research work. Few sanatoria are now equipped with first-class laboratories. Few medical superintendents have the time to make investigations on immunity problems, metabolism, fatigue, chemical pathology, blood pressure, etc. Great Britain has no great post-graduate sanatorium school like the Trudeau School of Tuberculosis in America. The vast amount of clinical material in sanatoria useful for research and teaching purposes is not made use of. The need for children's sanatoria must also be met. By concentrating sanatorium efforts on the next generation many potential cases of tuberculosis will be averted. Pulmonary tuberculosis is a slow, smouldering, chronic disease, and it is becoming more and more so as the result of the partial immunity of increasing urbanization, and perhaps also as the result of the more frequent and more effective treatment given. Chronic disease is a chronic expense. By making use of all appropriate preventive measures the need for sanatoria in the future will be greatly lessened.—*The Future of the Sanatorium, A. N. Robertson, Brit. J. Tuberc., July, 1921, xv, 115.*

Work of an After-Care Committee.—It is evident that no matter how complete an antituberculosis scheme may be, it will fail in the absence of some organization to assist patients who cannot remain resident in an institution and whose means are not sufficient to obtain a constant supply of all things needful for the maintenance of their impaired physical powers. To aid these people, "care committees" have been formed in various cities, and this paper gives an interesting account of the work done by the City of York Tuberculosis Crusade Committee formed in 1913. This Committee is supported by private subscriptions and money collected on an annual flower day. The work which the Committee attempts to carry on is as follows: (1) Provisional help for patients in need of immediate assistance; (2) extra nourishment; (3) friendly visiting and advice; (4) maintenance of patients while under treatment until able to work; (5) provision of separate beds, so that patients may sleep alone; (6) assistance with housework or washing while patient is in a sanatorium; (7) provision of deckchairs; (8) payment of removal expenses; (9) payment toward rent of larger houses to effect isolation of the patient; (10) provision of warm clothing; (11) expenses of boarding out in the country; (12) letters for convalescent homes, hospital, etc.; (13) provision of shelters; and (14) assistance toward cost of training for more suitable work. It is worthy of consideration whether it would not be true economy to prevent the development of active tuberculosis on these lines, rather than for the State to expend vast sums on sanatoria, training colonies, and village settlements for those in whom the disease is established. So far, this view does not seem to have appealed to the Ministry of Health, and no grants are available for such purposes. With more abundant funds at their disposal, Tuberculosis Care Committees can play a most important rôle in the campaign against tuberculosis.—*The Work of a Tuberculosis Care Committee, P. R. McNaught, Brit. J. Tuberc., July, 1921, xv, 118.*

The Course of Phthisis under Present Abnormal Environmental Conditions.—Underfeeding results in a loss of important parenchymal functions and predisposes to pulmonary disease. Primary infections are more common and new infections are occurring among sanatorium employees. The tuberculin treatment had to be discontinued in many cases on account of losses in weight. The new type of phthisis found in the last few years is conspicuous for the absence of bacilli in the sputum, in spite of the presence of other symptoms. All the cases have a negative family history, never had pulmonary trouble, and following influenza had a tired feeling, nightsweats and lost weight. Usually there is found infiltration of one or both upper lobes with sibilant râles throughout the lungs. After disappearance of the catarrhal signs, a circumscribed area presents crackling râles and the sputum is copious, purulent and without bacilli, even after repeated antiformin tests. The Pirquet test is always negative and the intracutaneous test only mildly positive. In one case bacilli did not appear until after repeated hemorrhages. In another, death occurred from bilateral caseous pneumonia thirteen days after a severe hemorrhage and the appearance of bacilli.—*Einige Besonderheiten im Verlauf der Phthisis Pulmonum nuter den jetztigen abnormen Verhältnissen, R. Güterbock, Berl. klin. Wchnschr., March 7, 1921, lviii, 232.*

Factors in the Spread of the Tubercle Bacillus.—The author is of the opinion that too much attention is being paid to the rôle of intermediary objects in the transmission of infection, and that the part played by direct transfer from open cases to infants is being slighted. A series of case histories is given of infants entering hospitals where they could be watched over a period of months and repeatedly tested with tuberculin, who were admitted in a nonreacting condition and later acquired infection. The infections were traced to direct contact. Without committing himself on the manner in which infection is acquired, whether it be by inhalation or deposition on mucous membranes with subsequent swallowing, Arnould makes a plea for an educational campaign on hygiene directed toward the elimination of too early or too frequent contacts between children and the tuberculous.—*Circonstances et conditions exterieures de la contagion par le bacille tuberculeux, E. Arnould, Rev. d. la tuberc., June, 1921, 3rd series, ii, 187.*

Experimental Contribution on the Relationship Between Phlyctenulae and Tuberculosis.—Previous experiments performed by Guillery demonstrated that various nonspecific ferments, injected intravenously or intraocularly, showed a selective activity for the uveal tract in all three of its parts. Within an hour after such injections the uvea reacted with marked vascular injection and focal collections of epithelioid cells and lymphocytes. Such reactions, without evidence of caseation and without the presence of any organisms, he considers as "tuberculoid" in nature, and entirely analogous in structure and appearance to phlyctenules. Similar series of reactions were obtained by the local or intravenous injection of tuberculin into the eye of a tuberculous animal or one previously treated by subcutaneous injections of tuberculin. Such reactions did not occur in an animal free from tuberculosis. The response is not specific, however, as local applications of staphylococcus toxins, or even the presence of head lice will cause similar ocular lesions. No explanation of the selection by these different substances of the uveal tract can be offered. Phlyctenular conjunctivitis is related to the so called scrofulous and tuberculoid processes, which show a cellular reaction similar to that of the tubercle, but in which tubercle bacilli are very rare or entirely absent. A short discussion of nonbacillary lesions and the possibility of the destruction of the tubercle bacillus by the body fluids is followed by the suggestion that it is possible for such lesions to be produced by toxins from the tubercle bacillus without the presence of bacilli at the point.—*Experimenteller Beitrag zu den Beziehung zwischen Phlyktanen und Tuberkulose, nebst Bermerkungen uber abazillare Tuberkulose, Guillery, Münch. med. Wchnschr., February 18, 1921, lxviii, 201.*

Relation of Childhood Tuberculous Infection to Adult Tuberculosis.—The author refers to the former dictum of von

Behring that the suckling's milk is the principal source of tuberculosis, and to the experimental work of von Behring's assistant, Roemer, who has been the exponent of childhood infection without exogenous reinfection in adult life, owing to the immunity conferred by first infection. He disputes such a conclusion, which he notes had a number of adherents at the recent German tuberculosis congress. On the ground of pathological observations, childhood infection cannot be the immediate cause of adult tuberculosis. The majority of early childhood infections result fatally, or they entirely heal; leaving behind only remains which cannot be regarded as sources of further danger. It is true, however, that the allergy resulting from the early infection can produce a different reaction to future infections and be a source of resistance to ward off to a great extent any further infections. On the other hand, frequent small infections occurring throughout adult life are sufficient to account for the resulting chronic pulmonary tuberculosis; the reason being that there are many predisposing causes which enter into the problem and assist in producing lowered resistance when infection happens to be present. It is not necessary to have massive infection to produce pulmonary tuberculosis, since a slight infection in the presence of debilitating influences, whether due to disease, physical or mental strain, may open the way and permit gradual reinfection. The acute types of tuberculosis, arising from primary infections, are characterized by caseous lymphatic nodes and other signs of lymphatic involvement in the regional nodes. This is the regular form of primary infection when unresisted and progressive, and is not seen in the ordinary adult type. In 1200 sections of soldiers in the field he encountered only five cases of tuberculous primary disease in adults. A certain few of these primary cases are found in Germany from the rural districts, but occur chiefly in negroes from the colonies. Chronic pulmonary tuberculosis can be seen occasionally in young children. These are undoubtedly secondary infections. Primary infections dating from the age of puberty are likely to be unresisted because of the many strains occurring at that period of rapid growth. They are, however, comparatively seldom. Therefore, while this childhood infection does give rise to a certain amount of immunity, it is by no means sufficient, nor would it be for this reason feasible to use a harmless tubercle bacillus for immunization and thereby obtain protection against future infection. The example of vaccination against variola is hardly applicable to tuberculosis, because the infection is brief and exposure infrequent in variola, whereas in tuberculosis there is a period of several weeks after vaccination, during the "negative phase," wherein a protection against infection could not be obtained in the majority of exposed infants. Furthermore, a nonvirulent vaccine for inoculation has not yet been discovered. The outlook for prophylaxis by immunization is not hopeful, because the artificially created allergy is no certain protection against reinfection and pulmonary phthisis.—*Über das Verhaltniss der kindlichen tuberkulösen Infektion zur Schwindsucht der Erwachsenen, H. Beitzke, Berl. klin. Wchnschr., August 8, 1921, lviii, 912.*

The Pulmonary Tubercle of Infancy.—Infection by the tubercle bacillus appears to be nearly always a result of inhalation, and the primitive tubercle seems nearly always to be formed in the lung during infancy. Pulmonary tuberculosis of the adult is usually a recrudescence of a latent infantile process. The beginning signs of pulmonary tuberculosis in an infant should not always be sought at the apices; they often appear at the bases. The lesions occur under different forms, and may be both nodules and tuberculous pneumonias. The nodule is the most frequent form of the primitive lesion. It is generally single and its size varies from that of a grain of wheat to a cherry. In its neighborhood there is frequently a crop of miliary tubercles, which sometimes remain in the immediate vicinity and sometimes extend toward the hilum along the bronchial tree. The tubercles being avascular, the bacilli are transported only by migratory cells. But these soon lose their motility and become implanted. Or, if the migratory cells get into the lymphatics, they are arrested in the lymph nodes and tubercles are formed there. The inoculation tubercle varies in appearance according to whether it is active or healing. The active tubercle is caseous, without collagen. About it is a congested, sometimes hemorrhagic, zone which may be very large, and at times extend over the whole lung, simulating a pleurisy with effusion or a vast hepatization. Histologically, the lesion appears as an alveolitis with central caseous degeneration containing many bacilli but neither epithelioid nor giant cells. One or several caseous foci affecting an acinus, a lobule, or part of a lobule, betray a recent severe tuberculosis. The extensive degenerations which follow cause the formation of tiny cavities and the invasion of the bronchi and vessels. These changes are typical of the rapid generalized tuberculosis of young children. In older children the signs of healing are more frequent. The primitive focus retracts and an encysted fibrocaseous tubercle is formed. Scar tissue appears early. Ghon has described it in a six months' child, and the writer has seen a fibrous perinodular ring in a baby of ten weeks. Calcification also occurs early. Küss has described a primitive nodule, entirely calcified, in a child of eleven months. The initial tubercle is found ulcerated in more than a third of the cases. These lesions, often suspected, form a permanent source of reinfection. The tubercles which become retracted and calcified show as dark spots on the screen. Among 100 nontuberculous adults, 65 showed these spots. Their position varied, but forty-two times it was the base of the lung. Adenopathy was almost constant; examinations showed black ganglionic spots indicating a gangliopulmonary tuberculosis in regression. A relationship between the calcified nodules and the present condition of the patient could not be established. The question arises whether the primary lesion, after cicatrization, may be the seat of a bacillary reactivation, and thus become a source of reinfection. Cases are seen in which it appears that active processes arise in an old nodule. But in most cases the primary tubercle shows no signs of virulence, although secondary lesions are in full process of development, but perish as a cicatrized or calcified nodule, remaining, like a vaccination scar, an evidence of early inoculation. The anatomical distribution appears to be inoculation tubercle, often at the base of the lungs, adenopathy at the hilum, and then secondary infection at the apex. Unlike the primary tubercle, the nodules at the apex tend to spread more extensively and to produce more important lesions. If the lungs of children and of youths at different ages be compared, it can be seen that in infancy, particularly in the first year, the rapidly developing tuberculosis has grown upon new soil not yet vaccinated. In adults, the slow development of a tuberculosis, with processes which tend to eliminate the bacteria and their poisonous products, is to be explained as growth in a region already modified and protected by previous infection.—*Le tubercle d'inoculation pulmonaire infantile et son évolution, L. Ribadeau-Dumas, Rev. d. l. tuberc., 1921, ii, 27.*

Open Pulmonary Tuberculosis in Infants.—Klotz would consider all cases in infants which show clinical signs of pulmonary tuberculosis as open, whether bacilli can be detected in the sputum or not. The sputum is hard to obtain, even when irritants like ammonia are inhaled. Repeated examinations of sputum so obtained are often negative. The lack of guinea pigs for diagnostic purposes in Germany has prohibited their use. The stools, moreover, have failed to show tubercle bacilli. He cites a case of this kind which undoubtedly infected three adult attendants and five other children. He believes these cases especially dangerous because of the high position and shortness of the infantile larynx, which retains little of the sputum and favors droplet infection by allowing quantities of bacilli to pass at once to the exterior with any violent expiration.—*Zur Frage der offenen, Lugentuberkulose im Säuglingsalter, Klotz, Münch. med. Wchnschr., August 13, 1920, lxvii, 964.*

An Unusual Case of Tuberculosis in an Infant.—The patient, a child eleven months old, was seen but once. The diagnosis would in all probability have been bronchopneumonia, had it not been for the history elicited. There had been exposure to pertussis. The child had alternately spent a week first with the paternal grandmother, who had tuberculosis, and with the maternal grandfather who recently died from the disease. A great-aunt of the baby also died of tuberculosis a few years ago. The writer after seeing the child once was called away on a business trip. Upon his return he learned the baby had died. The examination of the sputum by the laboratories of the State Board of Health showed the presence of tubercle bacilli.—*An Unusual Case of Tuberculosis, O. R. Stuteville, Kentucky M. J., May, 1921, xix, 228.*

The War and Tuberculosis Among the Children of Munich.—Analyis of the histories of 1940 patients at the University pediatrics clinic from 1912 to 1919, inclusive, showed that the incidence of positive Pirquet reactions occurred earlier in life during the years of the war than in those which preceded. The tuberculosis death rate among children throughout the whole city of Munich increased during the year 1916, while the rate for adults did not. This increase was confined chiefly to the ages between one and five. In 1917 the figures sank below those of 1914, and continued to fall during 1918 and 1919, although more slowly than in peace years. A possible explanation of the sudden increase is suggested by the fact that the previous two years of the war had brought to light many open cases of tuberculosis in adults. While all the able-bodied were engaged in military service the care of children was often left to the sick. In the later years of the war these conditions were remedied; children were brought into the country, and their diet was carefully provided for, even at a sacrifice on the mother's part. The children of Munich were more fortunate than those of other German cities, but it is to be feared that when these children, infected so early in life, reach school age, severe forms of tuberculous disease may occur.—*Über die Einwirkung der Kriegsverhältnisse auf die Tuberkulosehäufigkeit unter den Münchener Kinder, J. Bartschmid, Münch. med. Wchnschr., August 13, 1920, lxvii, 957.*

Abdominal Tuberculosis in Children.—*Summary:* 1. The diagnosis of primary abdominal tuberculosis in children is often difficult. 2. The variety of its types of manifestation has led to confusion in its treatment. 3. Hygiene, diet and outdoor life is the foundation of all treatment. 4. In the stage of localized mesenteric adenitis, surgical excision is logical, successful, and probably prevents the other stages developing. 5. In the ascitic stage laparotomy with evacuation of fluid is to be recommended when the patient fails to respond to medical treatment after a reasonable length of time. 6. The prognosis in the extensive adhesive stage is poor with any treatment, and operation is resorted to only for the hope of relieving obstruction in which it has been occasionally successful.—*Surgical Aspects of Abdominal Tuberculosis in Children, W. E. Ladd, Boston M. & S. J., September 15, 1921, clxxxv, 317.*

Tuberculosis in Old Age.—Tuberculosis in old people is considered in its bearing on the spread of the disease. In spite of a prevalent opinion to the contrary, tuberculosis in old age is almost as common as in adults of middle age, and figures to almost the same extent in the mortality column. In America (1910), for 10,000 males living at the age given, 23.57 between 45 and 65 years of age died from tuberculosis, while above 65 years the rate was 20.4. In Japan (1917) the rates for these periods were 18.2 and 15.6 respectively. In France (1906–1913) the rate from 40 to 59 was 53.6 and from 60 up, 33.5. In England the rate from 45 to 65 was 22.54, and from 65 up, 11.9. These figures are all for males; the rate among females was in all cases somewhat less. It is pointed out that in England, which shows the lowest senile death rate from tuberculosis, the mortality from "chronic bronchitis" is by far the highest. The implication is that the figure for chronic bronchitis includes much tuberculosis. Emphasis is laid by the authors on the dangerous place held by the senile consumptive, whose process is so mild and chronic as not to excite suspicion as to its real nature, and who thus becomes an unsuspected disseminator of bacilli.—*Fréquence de la tuberculose pulmonaire senile, A. Courcoux and P. Labesse, Rev. d. l. tuberc., June, 1921, 3rd series, ii, 196.*

Vaccination of Cattle.—The greater number of animals subjected to permanent residence in an infected area react positively to tuberculin in the first five years of their existence. Were all these animals permitted to grow old, all of them would show tuberculous lesions at the time of their natural death. It is, therefore, interesting to try to discover whether it is possible, by utilizing the young cattle, to confer on these animals a sufficient resistance to the natural infection so that they can, while living in close contact with the adult tuberculous cows, escape the infection spontaneously produced in the infected stables. The numerous experiments which have been made during the last twenty years by various investigators have not produced satisfactory results. The author in collaboration with C. Guérin undertook a number of experiments which proved that to obtain the immunity of the organism to bacillary infections, such as are spontaneously manifested in young people who have been healed of a benign tuberculous infection, it is necessary for the body to remain infected by bacilli, but that these bacilli should not produce follicular lesions or tend to the formation of tubercles. They succeeded in obtaining a culture of bacilli of very feeble virulence for small laboratory animals which can be injected intravenously without producing tubercles. It is this bile-treated bacillus, nontuberculined, and lowered to a dose of several mgm. for the rabbit, guinea pig, monkey, and man, that they use for their experiments in the vaccination of young calves. During the first days after birth, they inject at least 20 mgm. of a living culture of their bacilli, and leave the young cattle thus treated in intimate contact in the stable with cows suffering from open tuberculous lesions. Their conclusions, up to the present, show that these are well tolerated by the lymphatic system, that they produce no follicular lesions, and that they determine a manifest resistance, not only to the natural infections of cohabitation, but even to the infections provoked by intravenous experimental inoculation of tested virulent bacilli. The duration of the resistance has not yet been established. It hardly seems to extend to over a year, and it persists only as long as the bile-treated bacilli remain in the organism. When these bacilli have been eliminated by the natural channels of excretion, principally by the bile and intestines, the animals again become sensitive to tuberculous infection, but then vaccination can be renewed without harm. They have repeated it as often as three times in the same animal in three years, and then the resistance to natural infection has been maintained for an equal lapse of time. These men hope by analogous procedure to realize the immunization of young children, directly after their birth, in such a manner that they could resist family contamination for the whole period of their existence. Only an experiment on young anthropoid apes, in a region free from tuberculosis, can give an opportunity of verifying this hypothesis. This they propose doing as soon as they can gather together the necessary means.—*The Vaccination of Cattle Against Tuberculosis, A. Calmette, Brit. J. Tuberc., July, 1921, xv, 103.*

Latent Tuberculosis.—There exists a form of invalidism, fairly frequent, for which the author proposes the term, chronic bacillary state. Its essential constant elements are (1) subfebrile temperature, lasting for months or years, (2) chronic valetudinarianism, (3) family history of actual or suspected tuberculosis and (4) indefinite latency of suspected lesions. The temperature usually oscillates from 99° in the morning to 99.7° or 100° in the evening, but at times it is capricious, describing sometimes a curve from 96° to 100°, sometimes remaining in the neighborhood of 99°. In women there is almost always a positive febrile period (99.2° to 100.4°) from one to two weeks before menstruation. The fever is not modified by long rest, nor by exercise. It resists, or is only temporarily modified by antipyretics. The chronic invalidism is expressed in vague feelings of discomfort, weakness, fatigability, and sometimes headaches. There are often pains in the back, especially in the sacrolumbar region. In women there are nearly always menstrual troubles. There are often tachycardia, arhythmia, vague abdominal pains, diarrhea, and constipation. These patients often remain plump and have a good color. There is often, but not invariably, a family history of tuberculosis. Repeated thorough examinations elicit no authentic signs of tuberculosis. It may be that there are persons with very feeble powers of resistance who harbor tubercle bacilli of low virulence which they are unable to destroy or to segregate. In treatment, nothing is gained by imposing constant rest. When there is anemia, heliotherapy is useful, but it has no effect on the temperature. Tuberculin is the only remedy which occasionally controls the fever. The only hope for these patients seems to lie in growing old and thereby acquiring greater resistance.—*Tuberculose latente. Des états bacillaires chroniques, R. Burnand, Rev. d. l. tuberc., 1921, ii, 26.*

The Anatomic Forms of Pulmonary Tuberculosis.—The basis of this classification of lesions rests upon the anatomic structure of the lung. The primary unit is the lung lobule, composed of a small bronchus which divides into several respiratory bronchioles (small bronchi with alveoli opening directly into their walls). From the latter arise atria and sacculi alveolares. About the lung lobule is the perilobular connective tissue, from which strands pass into the lobule to form the framework of the alveolar wall. The vessels enter the apex of the lobule and their branches are distributed with the alveolar walls. According to Orth's most recent views the interstitial alveolar framework is a part of the parenchyma of the lung, while as stroma he allows only perilobular connective tissue. This point in nomenclature is important, because in the connective tissues of the alveolar walls, which are, however, parenchymatous, the tuberculous process originates. As Rindfleisch first noted, the most frequent seat of early tubercle is at the point where the respiratory bronchiole divides into its distal ramifications. On these facts a classification of lesions can be made. All tuberculous lesions may be subdivided into either proliferative changes starting in the alveolar framework, leading to the formation of tuberculous granulation tissue, or exudative processes involving the air spaces. These rarely exist in pure state, but are usually combined and the lesion is classified as one or the other process predominates. The proliferative type is characterized by the development within the alveolar framework of proliferative tubercle, which Orth has shown to be of fibroblastic origin. With this is the usual formation of giant cells, central necrosis and peripheral lymphocytic reaction. The lesion spreads by direct extension, and there is also a secondary increase in size due to inflammatory changes in the surrounding alveoli, a collateral and perifocal penumonia. The process may heal by encapsulation with connective tissue. It is due to the effect of implantation of tubercle bacilli within the connective tissue. The second type of process, exudation within the air spaces, is characterized by a proliferation and desquamation of the alveolar epithelium which fills the lumina with large mononuclear cells. These may undergo massive caseation, and the process is then known as caseous pneumonia. Frequently, according to A. Frankel, Tripier, Orth, and especially Colen, organization of such caseous exudate may result from the formation within the alveolar framework of granulation tissue, either tuberculous or nonspecific. This process is known as tuberculous carnification. The exudative and pneumonic processes are generally due to the action of the tubercle toxin rather than to the bacillus itself. Aside from these main headings Schmincke classifies lesions according to their morphological appearance and their method of spread, as miliary, nodular, and confluent types. The following distinct types are mentioned: A. Lesions of hematogenous origin: 1. Acute hematogenous disseminated miliary tuberculosis. This type is the result of a sudden rupture of a large number of bacilli into the circulation, and characterized by the appearance of widely distributed small discrete tubercles, situated in the stroma and parenchyma of the lung. The lesions are primarily proliferative, but are later increased in size by collateral and perifocal pneumonic exudation. Those at the apex are larger than elsewhere, probably due to the slower circulation in this region, which allows more bacilli to remain in the tissue. 2. A second type due to hematogenous dissemination is miliary caseous penumonia, the miliary caseous hepatization of Virchow. The primary lesion is of an exudative nature and localizes within a single acinus and then may spread to involve adjacent acini. As a result, there appear small nodular masses, often shaped like clover leaves, involving limited areas in the inferior portions of the lung. This type is most common in children. B. Nodular tuberculoses, usually processes spreading by way of the air passages: 1. Nodular proliferative form, due to proliferative lesions starting in the alveolar framework. Many such lesions may coalesce to form large nodules which frequently caseate. The intervening lung tissue may undergo a collapse induration, with a thickening of the collapsed alveolar walls and pigmentation due to secondary deposit of dust. 2. Nodular exudative form, due to a localized exudative process starting in the same location. Grossly, the nodule is not so sharply defined, due to the absence of a well-developed connective tissue capsule. Each of these processes tends to extend within the bronchioles toward the hilum, but during such spread the process becomes a mixture of exudative and proliferative reaction. It may extend through the wall of the bronchus, to involve its outer layers with the formation of a peribronchial tuberculosis, and it may spread still further to involve the nearby parenchyma. If caseation occurs over a considerable area of such involvement cavity formation results. "By aspiration of caseous material into other portions of the bronchial tree new nodular exudative lesions are formed." These nodular types tend to invade vessels. Those of a proliferative nature often invade the lymphatics and set up local metastases. Frequently the exudative type involves perivascular lymphatics, with an extension to the intima of the blood vessels and possible rupture into the circulation. C. In the third group are the confluent processes of both cirrhotic and pneumonic character: 1. The first type is thought to be due to the confluence of many nodular proliferative lesions involving an extensive area. The apical scars representing healed primary infections are probably of this origin. The type is characterized by a tendency to the formation of connective tissue which later retracts, resulting in deformity. Heavy pigmentation by dust and pleural adhesions is a usual complication. Cavity formation is not infrequent, and is often of bronchiectatic origin. 2. The confluent pneumonic type, galloping consumption or phthisis florida, may involve very large areas, even whole lobes. The parenchyma undergoes rapid softening with the formation of huge cavities; the stroma, with its vessels and bronchi, may persist as trabeculae traversing the walls and lumen of such a cavity. The vessels usually undergo thrombosis; if not, there is a strong tendency to aneurysm and hemorrhage. The prognosis is unfavorable in all types except the nodular and confluent proliferative.—*Die anatomische Formen der Lungentuberkulose*, *A. Schmincke*, *Münch. med. Wchnschr.*, *April, 1920, no. 14, 407.*

Pathology of the Pleural Endothelium.—An accident to one of the workers at the Sanatorium Mangini at Hauteville was followed by a traumatic pleuritis with a small sterile effusion, which furnished material for a study of changes in the proliferating endothelial cells. Such traumatic inflammations, which are likely to follow the distribution of intercostal nerves, are presumably the result of trophic changes, and represent no such great departure from normal conditions as an ordinary toxic inflammation. Thus, the cells which were the subject of this study may be looked upon as passing through changes which, if not entirely normal, were at least nearly so. Studied as a free cell in the pleural exudate, the endothelial cell of the pleura appears very different from the flattened irregularly polygonal cell pictured by histologists. In its detached form it is a regular spheroid with the nucleus at the smaller end. The fine chromatin granules of the nucleus, which stain a dark violet blue with Giemsa stain, are so regularly arranged that the surface seems homogeneous. The nucleus is generally single, but some structures are seen which contain several nuclei. In some cells the protoplasm was packed with fine granules which stained a very intense violet blue. This basophilia, characteristic of young cells, was taken as proof of a good state of preservation. Their sizes varied from that of an ordinary lymphocyte to a large mononuclear. These differences in size were evidence of a process of new cell formation caused by the traumatic process. In certain other cells the cytoplasm differed from that of the first kind in the size and staining reactions of its granules. The color of these varied from violet blue to rose (Giemsa). Every shade of the color scale showed the slow gradual passage from basophilia, through neutrophilia, to acidophilia. The endothelial cell may, therefore, undergo two kinds of transformation, related, probably, to two different functions. Either the protoplasm becomes vacuolated and the cell becomes a macrophage, or the cytoplasm granules pass through modifications which end in a typical eosinophile. The latter transformation produces, doubtless, the pleural esoinophilia which the writers have seen in traumatic effusions of idiopathic origin. These facts indicate that the eosinophile cell is not a specific element derived from a definite organ or system, but that it arises by a special kind of differentiation of cell protoplasm and may have different origins. The plastic spheroidal form of the pleural cell helps to explain an obscure physiological phenomenon, namely, the change in volume, during respiration, of the endothelium of the visceral layer of the pleura. During inspiration the elastic basal layer is stretched, forcing the cells to elongate in their transverse axis and to shorten in their longitudinal axis; during expiration the opposite change take places. During pleural inflammation, turgescence of the cells, caused by peripleural edema, may cause their free ends to project into the pleural cavity. This may produce a roughening of the surface of the pleura which, when it rubs against the opposite layer, produces the pleuritic friction sounds. These sounds have been imputed to the presence of a fibrinous exudate, but the fibrin is too finely divided and too smooth to produce them. That they are due to friction of a dry granular surface seems attested by the fact that they disappear when the effusion is formed and reappear again at the moment of its reabsorption. The friction sounds may disappear because of the liquid interposed between the two layers of the pleura or because the secretion of liquid into the pleural cavity lowers the intracellular pressure and reduces the turgescence of the endothelial cells. During absorption of the exudate, intracellular tension rises again and the condition returns to which the friction sounds are due. The pressure on nerve endings due to turgescence is, no doubt, the cause of pain in a traumatic just as it is in an infectious pleuritis.—*Quelques remarques sur la morphologie et la physiologie pathologique de l'endothélium pleural, F. Dumarest and F. Pavodi, Rev. d. l. tuberc., 1921, ii, 44.*

Humoral Antibodies in Tuberculosis.—*Summary*: 1. The importance of the antigens is indisputable. Protein fraction of the antigen constitutes the strongest antigenic property. The best antigen used by us is the glycerin extract which we have modified of late. 2. Antigen and antibodies are colloids. 3. That complement fixation may occur, even without the appearance of a precipitate, cannot definitely be proved. Albumin particles may aggregate into larger particles without a precipitation, provided the excess of one of the precipitin-forming colloids acts as a protective colloid. On the other hand, it has not yet really been demonstrated that a physical fixation and not an irreversible chemical change occurs in complement fixation. 4. Antibodies are either globulins, or adsorbed and carried down with the globulin fraction. X-ray and ultraviolet rays have little effect in causing their destruction. Direct sunlight apparently destroys the antibodies in a short time. 5. An attempt was made to determine the electrical change of the antigen and the antibodies by the study of kataphoresis. Both being amphoteric colloids, they are influenced by the H- or OH-ion concentration and may move either to positive or negative pole. Their electrical charge is very small and for this reason either of these ions may reverse their electric charge. 6. Precipitins and agglutinins have been studied in tuberculosis. These two antibodies are closely related.—*Studies of Humoral Antibodies in Tuberculosis, S. A. Petroff and G. G. Ornstein, N. York State J. Med., August, 1921, xxi, 299.*

The Erythrocyte Volume in Tuberculosis.—The erythrocyte volume has been calculated in thirty-nine cases of pulmonary tuberculosis in various stages. These determinations were made both by the refractometric method of Bence and viscometric method of Adler. In addition, hemoglobin percentages, erythrocyte counts and plasma protein determinations are recorded. The erythrocyte volume shows a marked decrease in all these cases, and in severe fibrous and actively progressive cases the volume is reduced one-half or more. But some cases with severe disease show little disturbance of the red corpuscle volume, while others with a mild pulmonary involvement present an excessive decrease in this respect. A portion of the cases represent a simple oligemia, or deficiency in blood volume, due to the loss of fluid through night sweats and high fever. In others there is real injury to the erythropoietic system, the bone marrow. When the respiratory surface becomes reduced by cirrhotic disease of the lungs, the toxins of the infectious process injure the bone marrow and restrict red blood corpuscle production. There results an excess of carbon dioxide in the blood, which in turn stimulates the bone marrow, many new erythroctyes are formed, and the restricted respiratory surface is compensated by an excess of red cells. Thus may be explained the polycythemias of bronchiectasis, etc. If the bone marrow is insufficient, there arises not a polycythemia, but a blood of which the total number of red cells approaches normal, while the size of these cells will be much decreased. The bone marrow is capable, in other words, of producing a given amount of red corpuscles; it attempts to produce cells of a normal size; if deficient it will perhaps produce a larger number of cells, much reduced in size.—*Zur Frage des Erythrozytenvolumens bei Tuberkulose, H. Kammerer und L. Geisenhofer, Münch. med. Wchnschr., July 18, 1921, lxviii, 844.*

Methylene Blue Excretion in Tuberculosis.—Koch believed that small amounts of methylene blue, taken internally, are either destroyed by the liver or retained by it, if it is functionating normally, while an injured liver cannot act in this way and the dye is excreted in the urine. Two (up to 5) mgm. of methylene blue are taken and the urine examined hourly for the dye or its decomposition product called chromogen. Müller (*Arch. f. klin. Med., lxiii, 130*) has described eight stages and "leucoproducts" for methylene blue: 1. The unchanged dye, M. 2. Reduction leucoproduct, leucomethylene blue L. 3. The oxidation product coloring the urine green, $M\alpha$. 4. The bacterial leucoproduct of $M\alpha$. (found in urine that has stood or in cystitis.) $L\alpha$. 5. The chromogen appearing on boiling, $L\beta$. 6. The oxidation product of $L\beta$ produced by boiling, $M\beta$. 7. The chromogen formed by boiling M urine with acetic acid $L\gamma$. 8. The oxidation product of $L\gamma$ which is designated $M\gamma$. Tuberculosis cases revealed a marked power to destroy methylene blue in that within 6–10 hours no $M\alpha$, $L\beta$ or $L\gamma$ was excreted. If $M\alpha$ was excreted in some cases the excretion was markedly retarded. Turban II and III cases revealed this phenomenon. Cases of influenza also possessed this power, although not so consistently. Cases of chronic nephritis with polyuria also showed the same effect but the reason was probably not identical to that in tuberculosis. Lung, liver, spleen, kidney, muscle, lymph nodes and brain possessed the power to decompose the dye in dilutions of 1:5,000 to 1:100,000. Lung tissue was far more active than that of other organs. A discrepancy existed, however, in that blood also possessed this ability to destroy the dye while serum did not. Blood from cases of tuberculosis changed the dye more than blood in other diseases or from normal individuals. Heating did not destroy the power of ground up tissues to convert the methylene blue, while extraction with ether enhanced it. Tissues from diseased persons did not act differently from those from normal individuals. Tuberculous lung tissue, however, instantly changed the dye to a green-yellow or green-blue color, doing this much more rapidly than normal lung tissue. The absence or delayed secretion of the dye in tuberculosis may be accounted for by the marked affinity of this dye for the tubercle bacilli, by which it is "anchored" or this cumulation permits its destruction before being transported to the excretory organs.—*Über Methylenblauausscheidung bei Tuberkulose, R. Pfeiffer, Beitr. z. klin. d. Tuberk., March, 1921, xlvii, 46.*

Chronic Tonsillitis as a Source of Mixed Infection in Pulmonary Tuberculosis.—A case of chronic tonsillitis with advanced pulmonary tuberculosis is reported. The tonsillitis is looked upon as the source of the mixed infection, the secondary cocci disappearing from the sputum after removal of the tonsils and the clinical symptoms of mixed infections abating.—*Tonsillitis chron. als Ursache einer Mischinfektion bei einem Fall von Lungentuberkulose, E. Schulz, Beitr. z. klin. f. Tuberk., March 15, 1921, xlvii, I.*

Value of Finding the Early Case of Tuberculosis.—At the annual meeting of the Indiana Tuberculosis Association, January 27, 1921, the president in his address said that to successfully carry on the work to eradicate tuberculosis physicians must have the full and intelligent coöperation and support of the public. The public must be impressed with the importance of the war which the medical fraternity is waging against tuberculosis and be convinced that tuberculosis can be rooted out of the community. Public clinics held throughout the State would be potent factors in impressing upon the people the great prevalence of the disease. It is necessary to make all tuberculosis workers clearly understand that the prevention of tuberculosis is more of a general health problem than a narrow fight against this one infection. The public must be convinced of the great possibilities of this work and numbers of cases must be restored to their families and their employers, able to resume their civic duties and help bear the burdens of the community. To be able to so restore them, the physicians must find their cases early.—*Finding the Early Cases, E. Crull, Annual Meeting Indiana Tuberc. Ass., January 27, 1921.*

Early Diagnosis of Pulmonary Tuberculosis.—One of the early symptoms of tuberculosis is the facies of tuberculosis, most marked in children. Two types, the fairy and the manikin type, are seen, but most distinctive of the disease is the expression of thought in the child's face. Other early symptoms are the erethic temperament, loss of appetite, toxemic dyspepsia, dyspnea following ordinary exertion and pallor of the face, fauces and larynx. There may be local cyanosis and chilblains in cold weather. Amenorrhea is an early symptom. A mild intermittent pyrexia is of great value in diagnosis. Physical signs are delayed expansion with falling of the nipple on the right side of the chest, dystrophy of the trapezius, microadenopathy, diminished resonance over the right upper lobe, faulty tidal expansion at that apex, and a weakness of the inspiratory murmur. To prove the relation of these physical signs to the tubercle bacillus, tuberculin is invaluable. In certain cases the X-rays are a valuable adjunct to diagnosis, and may confirm or modify the signs as revealed by other clinical methods. Radioscopy is more valuable than radiography, because the earliest lung changes, reduced illumination and diminished expansion at an apex are never as well appreciated in a photographic plate as on the fluorescent screen.—*The Early Diagnosis of Pulmonary Tuberculosis, H. G. Sutherland, Confér. internat. contre la tuberc., October 17–21, 1920, 102.*

Early Diagnosis of Pulmonary Tuberculosis.—The increased incidence of tuberculosis following the war and the present economic conditions in Germany demand an early diagnosis of the condition. The patient is unable to pay for prolonged sanatorium treatment, and his absence from work has its effect upon industrial prosperity. The procedure for making an early diagnosis may be summarized as follows: By inspection, one determines whether the apical expansion is equal on the two sides, whether the acromion processes and clavicles are moving equally, and whether there is any deepening of the supra- and intraclavicular fossae. Inequality of the pupils may follow cervical lymph adenitis due to sympathetic excitation. Palpation may detect enlarged lymph nodes and muscular tension over a diseased apex. Threshold percussion is of greatest value in outlining the apical fields. Percussion should be performed not only with quiet breathing, but in deep inspiration and expiration, because in early apical disease the respiratory displacement is distributed. The percussion note over such areas is not only sharper and higher pitched, but very frequently there is a tympanitic ring. Auscultatory phenomena must be carefully analyzed. Inspiration can be weakened as well as sharpened. Expiration can be either normal or less prolonged. Most frequently it is prolonged and sharper, with a tendency to become bronchial. An apical scar can also give a sharp or even bronchial breathing. The X-ray is of little value in the diagnosis of early apical pulmonary tuberculosis, as the lesion may not be of sufficient size, or it may be of other than tuberculous origin. Tuberculin is of great importance in the early diagnosis, but for such diagnosis the focal reaction within the lung induced by its injection must be studied. The local reaction in the skin cannot differentiate between tuberculous infection and tuberculous disease and is therefore useless. By inflaming the lung focus the local signs will be increased and they can be followed by the methods of physical diagnosis. Moreover, there may be a general reaction which, in conjunction with the focal reaction, is of greatest significance.—*Die frühzeitige Feststellung der Lungentuberkulose, Litzner, Münch. med. Wchnschr., December 17, 1920, lxvii, 1469.*

Value of Auscultation in Early Diagnosis.—The chief problems are in cases with diminished vesicular breathing. After excluding cases due to rhinopharyngeal lesions, nervous and digestive troubles, visceral ptoses and other less frequent origins, it is a fact that constantly feeble breath sounds, located at the apex, are, in the great majority of cases, caused by tuberculous lesions, even though no bacteria can be found in the sputum. These lesions are generally not very active; they may become less active or latent, but their future can not be predicted from the bare auditory finding. Can the breathing in such cases be distinguished from that of a pulmonary atelectasis? Not with certainty, although in the tuberculous lesion there is generally some roughness associated with the respiratory sound. Feeble breath sounds only exceptionally indicate a beginning tuberculosis. Decrease of the vesicular murmur was coincident with tuberculous evolution in only a tenth of the writer's cases, and even in these the sound was not caused by a recent lesion, but by an old lesion which had served as a source of reinfection. These latent lesions may be rich in bacilli, which are encysted, as in large tubercles walled in by fibrous tissue. In children and adolescents feeble breath sounds are more often due to gangliopulmonary than to simple pulmonary lesions. The greater incidence of tuberculosis in the right than in the left bronchial lymph nodes accounts in part for the greater frequency of feeble breathing in the right than in the left apex. Most of the cases with feeble breath sounds show no evolution toward phthisis, only alternating periods of gain and loss in weight and strength. More than half of them have had hemoptysis, often recurrent. Some had a first hemorrhage ten or more years back. Feeble breath sounds are almost never a sign of beginning, and must not be taken to indicate healed tuberculosis. In doubtful cases with feeble breath sounds X-ray evidence is important but not infallible. A cured or an arrested lesion nearly always increases the cloudiness on the screen, but it may also be that X-ray evidence is negative in cases of undoubted tuberculosis, either because the lesion is too small or because it is marked by a considerable zone of emphysema. Disagreement between X-ray and auscultatory findings should lead to a renewed search for functional origin of diminished breathing. Rough localized breathing indicates a pulmonary lesion. Fewer mistakes are made in regard to rough than in regard to feeble breath sounds. Rough diminished breathing must be distinguished from rough increased breathing. The former indicates parenchymatous lesion of the lung, without prejudgment as to the activity of the process. It is not rare to find bacilli in the sputum of such cases. Such rough breathing may persist for years, but it may also be replaced by sibilant breathing, accompanied by crepitations. X-ray examination in cases of rough, diminished breathing generally shows a marked decrease in clearness at the apex. There are often cases where rough breathing is heard at one apex and feeble at the other. When these sounds are not marked some examiners will attribute the lesion to one side, some to the other. The decreased vesicular murmur on the other side may be caused by a pleuritis too mild to produce a shadow, or to a mixture of slight sclerosis and emphysema. Dry, granular, grating sounds are but varieties of rough breathing, and should not be mistaken for râles or crackling sounds. The same is true of cogwheel respiration. At the beginning of an exacerbation other sounds appear. These are either transitory, movable subcrepitant râles or crackling sounds, especially in the supraspinous fossa and under the clavicle.—*La valeur de l'auscultation pour le dépistage précoce de la tuberculose pulmonaire chronique de l'adulte, F. Bezançon, Rev. d. l. tuberc., 1920, i, 1.*

Which Lung is Most Frequently Involved in Tuberculosis?—After summarizing the observations of Strandgaard at Boserup and of Cavalcanti at Davos, Mayer proceeds to analyze the first 2500 cases from Turban's Sanatorium. His results in the main corresponded with those of the other observers. The rightsided lesions slightly outnumbered the left. The predilection of the right apex for tuberculosis is the result of the asymmetrical branching of the vessels and bronchi in a three-lobed lung, where, because of poor aeration the retention of pathogenic microörganisms, once they have gained access to the lung, is favored, and because of poor circulation disease once started becomes progressive.—*Welche Lunge erkrankt am häufigsten an Tuberkulose? A. E. Mayer, Münch. med. Wchnschr., August 6, 1920, lxvii, 935.*

Differential Diagnosis of Caseous Pneumonia and Proliferative Phthisis.—According to Ballin, the elastic fibres in the sputum in proliferative phthisis with a tendency toward induration lie in bundles or are arranged irregularly, while in caseous pneumonia as well as in pulmonary gangrene or abscess the alveolar structure of the elastic fibre is preserved. This was confirmed in a postmortem study of ten progressive cases. In cases revealing both fibres in bundles and alveolar structural arrangement a combination of indurative phthisis and caseous pneumonia was disclosed. The method of examination is to mix 10 cc. of sputum with 10 cc. of 10 per cent potassium hydroxide, shake several times and heat to complete liquefaction, add 60 cc. distilled water and centrifugate. The elastic fibres are found in the sediment.—*Ein Beitrag zur Differentialdiagnose* *der käsigen Pneumonie und der producktiven Tuberkulose nach der Ballinschen Methode, K. Freundlich, Berl. klin. Wchnschr., April 11, 1921, lviii, 351.*

The Detection of Tubercle Bacilli by Dark Field Illumination.—Sputum smears stained by the Ziehl method when examined under dark field illumination present bacilli stained bright green, lying on a dark or yellowish brown background. The characteristic beading of slender bacilli, lying often in bundles, is sufficient to identify the organism. Their identity has been confirmed by the employment of the new Zeiss rotating light and dark field condenser. The dark field method, because of its greater penetration, detects bacilli in thick smears or poorly stained bacilli which would escape detection by direct illumination. Moreover, where few bacilli are present, the method offers a ready means for their detection. Attempts to detect the "negative phase" of the tubercle bacillus by this method have failed.—*Über die Benutzung des Hoffmannschen Leuchtbildsverfahren zum Studium von Mikroorganismen, insbesondere zum Nachweis von Tuberkelbazillen in fixierten, gefarbten Praparaten, E. Keining, Münch. med. Wchnschr., February 4, 1921, lxviii, 131.*

Ambard's Coefficient in Pulmonary Tuberculosis.—In nonfibrous pulmonary tuberculosis the ratio of the urine urea to the blood urea may be normal, diminished or increased. The last condition is the most frequent. Increase of the ratio occurs especially in exacerbations, decrease especially in advanced stages. In fibrous tuberculosis the increase of the azotemia and of the secretory constant is frequently due to changes in the kidney and is a quantitative indication of their extent. The same conditions may occur in fibrocaseous tuberculosis. In peritoneal tuberculosis with ascites, there may be a rise in the constant, due to mechanical compression. But a rise in the constant is, perhaps, most often caused by those functional disturbances which result from acute infections. This is shown by the fact that with the improvement of the acute condition constant falls or returns to normal A rise in the secretory constant may be coincident with a normal elimination of methylene blue and an almost normal power of urea concentration. The elimination of nitrogen tends to remain high in the tuberculous, even up to the approach of death, and even if the food nitrogen is low. This intensity of nitrogen elimination undoubtedly tends to produce an increase in urea and in the secretory constant. A fall in urea and a lowering of the constant does not always appear to be due to amyloid degeneration, as Kindberg believes. Generalized amyloid degeneration in pulmonary tuberculosis is comparatively rare, and the lowering of the secretory constant relatively frequent. There does not seem sufficient reason to attribute this lowering to modifications in renal permeability. There may be in tuberculosis a state of kidney hyperfunction which manifests itself in the marked elimination of chlorine and phosphorus, and, perhaps, of urea.—*Azotémie et coefficient uréo-sécrétoire chez les tuberculeux pulmonaires, M. P. Weil, Rev. d. l. tuberc., 1921, ii, 110.*

Blood Sugar and Basal Metabolism Findings in Chronic Pulmonary Tuberculosis and Hyperthyroidism.—McBrayer reports the results of studies that the laboratories of the North Carolina State Sanatorium have been pursuing during the current year on the differential diagnosis of incipient pulmonary tuberculosis and incipient hyperthyroidism. The studies have been made on twenty-three incipient, seventeen moderately advanced and four far advanced cases, along with six known nontuberculous persons. The conclusion reached as a result of these studies was that the determinations of basal metabolic rate and blood sugar are of no practical value in the differential diagnosis of chronic pulmonary tuberculosis and hyperthyroidism.—*Blood Sugar and Basal Metabolism Findings in Chronic Pulmonary Tuberculosis and Hyperthyroidism, R. A. McBrayer, J. Am. M. Ass., September 10, 1921, lxxvii, 861.*

Sochanski's Method of Differentiating Exudates from Transudates.—An exudate in 1 cc. amount mixed with 9 cc. of Sochanski's reagent (1 cc. of 1 per cent phenolphthalein with 1 cc. N/10 sodium hydroxide in 98 cc. of distilled water) decolorizes the reagent while a transudate in the same amount will not. The neutralizing point of any fluid may be determined by using varying amounts (0.2, 0.3, 0.4, etc.) of the reagent and thus changes in pleural fluids observed. Transudates decolorize amounts below 1 cc. of the reagent, some even as low as 0.2 cc., by this graded method, while purulent exudates always decolorize amounts in excess of 1 cc. These results were obtained in examining 38 specimens. Determination of the amount of nitrogen in the titrated specimens revealed no relation between the neutralization of sodium hydroxide and the amount of protein as was claimed by Martini.—*Sochanski's Verfahren zur Unterscheidung von Exudaten und Transudaten, R. B. Larsen and K. Secher, Berl. klin. Wchnschr., March 28, 1921, lviii, 299.*

X-ray Examination of the Chest.—The object of this paper is to bring before the profession a practical method of X-ray examination of the chest, based upon 10,000 such examinations, each checked by careful physical examination and history or autopsy, and to present the X-ray classification of tuberculosis used at the Cincinnati Tuberculosis Sanatorium. The primary purpose of the examination is to locate and describe abnormal densities and thus detect tuberculosis, identify its type, and differentiate it from other chest lesions. Physical signs may disappear, but the X-ray will always disclose an area of healed tuberculosis. The fluoroscope cannot compare with the stereoscopic chest plates in detecting slight lesions, nor in studying the pathology of gross tuberculous lesions. Its value lies in studying motion. The movement of the diaphragm, the pulsation of the heart and aorta, the posterior mediastinal space, and the passing of the barium bolus through the esophagus can be best studied by the fluoroscope. Before reading and interpreting lung plates it is necessary to understand the normal plate, or rather, the average plate of normal individuals, at various ages. Almost every scar and calcified area within the lung leaves a mark upon the plate, and as all adults have such areas they must be recognized at their true value. The author has found proof beyond question that pulmonary tuberculosis is not always present when tubercle bacilli are reported in the sputum. In 8 of the 10,000 examinations above mentioned, 2 proved to be acid-fast bacilli other than tubercle bacilli; and 6 were due to old nodes rupturing into a bronchus, from which large numbers of bacilli were expelled for a few days and then were found no more. No evidence of lung involvement was ever found. The author gives an X-ray classification of pulmonary tuberculosis. The author concludes by asserting the need for a more general use of the X-ray in studying the lungs. If such study were made a part of the general routine it would not be long before many problems, such as syphilis of the lung, would be more fully understood. The greatest value of the routine X-ray examination lies in its ability to yield definite data in the absence of definite physical signs.—*X-ray Examination of the Chest and an X-ray Classification of Pulmonary Tuberculosis, H. K. Dunham, Am. J. Roentgenol., August, 1921, viii, 427.*

The Nature of the Tuberculin Reaction.—The tuberculin reaction is not an antibody reaction. Proof of this lies in the fact that tuberculin mixed with complement and emulsions or extracts of tuberculous organs is not toxic for normal guinea pigs, as it would be were it modified by the action of tissue antibodies upon it. It is not an antigen; for immunization with it does not protect against the normal lethal dose. Sensitivity to it is not transmitted passively, being a function of the whole allergic body. This sensitivity is produced only by infection with living bacilli. The anaphylactic state as respects tubercle bacillus protein may be produced by injection of dead bacilli, but this has nothing to do with sensitiveness to tuberculin. Tuberculin stimulates reaction in the sensitized body without necessarily being itself changed in the process. Tubercle bacilli entering the body exert the same action and are rendered harmless by the specific reaction.—*Über das Wesen der Tuberkulinreaktion, H. Selter, Ztschr. f. Immunitätsforsch. u. exper. Therap., June 20, 1921, xxxii, no. 1.*

A Diagnostic Tuberculin.—In doing routine diagnostic tuberculin tests in his clinic, Moro noticed a sudden falling off in the number of positive reactions. On checking up this phenomenon by the use of five different makes of tuberculin, he found that while some products gave strong reactions, others gave either very weak ones or none at all on the same individual. All these products were presumably of standard strength, as they had been stamped "government tested," but investigation showed that this test consisted in the injection of a given amount of the product in question into a tuberculous guinea pig. If the pig died within twenty-four hours the tuberculin was approved and put on the market. But such a test has no significance, for what may answer for guinea pig research may be entirely impotent as far as the human skin is concerned. Substances like *cutine* must be present in a tuberculin in order that it may give reactions in the human skin. Therefore a clinical test is also necessary before the product is put on the market for diagnostic purposes. Experiment showed that cultures with the most prolific growth yielded the most potent tuberculin, and further, that a partial concentration of the old tuberculin increased its reactivity. Moreover, some children with pure bovine infections would react to bovotuberculin only, and others with pure bovine infections reacted to tuberculin of human origin only; but owing to the far greater preponderance of bovine infections the human tuberculin was of greatest value. The author then devised a tuberculin the composition of which he summarized as being "old tuberculin, made from selected stock cultures, partially concentrated, containing a certain proportion of bovotuberculin, and strongly enriched with cutine." This product he has used for some months with entire satisfaction.—*Über ein diagnostische Tuberkulin, E. Moro, Münch. med. Wchnschr., October 29, 1920, lxvii, 1254.*

Diagnostic Tuberculin Inunction.—Experience in the Heidelberg clinic has shown that as far as sensitiveness is concerned, inunction with a diagnostic tuberculin salve is not surpassed by Pirquet's scarification method. No case has been observed where a negative reaction by inunction was followed by a positive Pirquet reaction. The salve is made with the new diagnostic tuberculin (d. T) concentrated to one-half its original volume according to the method of Hamburger and Stradner. Two parts of this tuberculin are mixed with one part of anhydrous lanolin. When employed in this way without lanolin, a reaction can also be obtained, but this is not as intense, as the lanolin tends to hold the tuberculin in the deeper layers of the skin for some time, thus producing a more lasting effect.—*Die Perkutanreaktion mit diagnostischem Tuberkulin, E. Moro, Münch. med. Wchnschr., March 25, 1921, lxviii, 364.*

The Subcutaneous Tuberculin Test.—During the years 1911, 1912 and 1913, a considerable number of patients admitted to the King Edward VII Sanatorium as cases of pulmonary tuberculosis, but with sputum which was uniformly free from tubercle bacilli, were subjected to the subcutaneous tuberculin test. This paper gives a detailed report of 100 consecutive cases thus tested, as well as the after-histories of these patients as ascertained in 1915 and again in 1920, and draws the following conclusions: Failure to react to tuberculin does not exclude tuberculous disease. A negative response, however, would appear to indicate that tuberculous disease, if present, is quiescent and does not call for active treatment. When the general clinical picture of a patient strongly suggests pulmonary tuberculosis, a negative response should be ignored. A general or febrile reaction alone gives no useful information and has no diagnostic significance. A focal reaction indicates the existence of a tuberculous lesion. This reaction is of much less significance, from the point of view of diagnosis and treatment, than the presence of tubercle bacilli in the sputum. It is in patients in whom a positive diagnosis can be made with some confidence upon general clinical grounds that the focal reaction is most likely to be obtained. In practice, however, the test is indicated in few, if any, of these cases. For a focal reaction, should it occur, but confirms the diagnosis already made, while the absence of the reaction does not in any way discount a positive diagnosis. If, as should be the case, the subcutaneous test is applied only to those patients in whom, after full investigation, the diagnosis still remains uncertain, the most informative response to the inoculations, namely, the focal reaction, is scarcely ever obtained. In short, it is in the cases in which assistance is most needed that the tuberculin test is least likely to give any indication. The test is not a means whereby the existence or absence of tuberculous disease can be determined. Neither, when a tuberculous lesion is present, does the test give any information as to its activity. Brown and Heise have arrived at substantially the same conclusions. The test has disadvantages in that the general reaction so often produced gives rise to discomfort and unpleasant symptoms. Further, in unskilled hands, the test may do definite harm.—*The Subcutaneous Tuberculin Test, N. Bardswell, Tubercle, July, 1921, ii, 433.*

Tuberculin in Determining Activity.—In 1916 Preiss did intracutaneous tuberculin tests, using a minimal dose on a number of cases with unquestionable pulmonary tuberculosis. With fresh active cases the injection was followed in a few hours by a marked local reaction and a slight general reaction. The former consisted of erythema and induration, which appeared early and persisted for at least two days. In four days all traces of reaction had disappeared. Three years later he again saw four of these same cases, of which three were clinical cures. He again repeated the intracutaneous tests, using the same doses. In the three healed cases the reaction progressed to its maximum, as before, but instead of disappearing in four days a palpable nodule was present in one after two weeks and in another after seven weeks. The case, still showing clinical activity, reacted as before. He therefore concludes that intracutaneous tuberculin is of definite value as an index of activity.—*Zur Unterscheidung eines aktiven von einem inaktiven tuberkulosen Herd, L. Preiss, Münch. med. Wchnschr., May 13, 1921, lxviii, 583.*

Fever in Tuberculosis.—No one can be cured of tuberculosis until he is afebrile. No one capable of becoming febrile on taking a normal amount of exercise can be regarded as cured. Fever indicates activity of the disease. The most important point in treating pulmonary tuberculosis which tends to be autotoxic is to prevent the tissues from being seriously injured by too much toxin. This can usually be done by putting the patient to bed, and especially applies to early cases. If an effort is to be made to bring about a cure by a reaction produced either by exercise or the injection of tuberculin, then it must be comparatively transitory in duration; otherwise the patient will be like one suffering from acute disease and irrevocable damage may be done to the lung. It would appear that in some cases where tuberculin has been given without proper control, a cure or the reverse has often been merely a matter of chance. Chronic cases always present difficulty and are as a rule due to neglect of rest in the early stages; they might be roughly defined as cases which have lost their sensitiveness to toxin. From experience it is known that rest in these cases is extremely beneficial. The few brilliant results obtained by giving big doses to these cases are a very poor guide as to the correct method of giving tuberculin. In hilum or lymph node tubercle occurring in children, the necessity for complete rest or for a modified amount of exercise can be gauged from symptoms rather than from temperatures. If these patients gain weight, cease to sweat, cease to be tired and do not complain of headaches and improve generally, then a certain amount of exercise is indicated; though the writer has always found the ultimate prognosis much better when it has been possible by any means to produce a normal temperature with a 36.5°C. temperature early in the morning.—*Fever and Temperatures in Pulmonary Tuberculosis, E. E. Prest, Tubercle, July, 1921, ii, 444.*

Tuberculous Hemorrhages.—The authors modify their previous classification: 1. Initial hemorrhages: (a) the only sign of a tuberculosis previously latent, which from that point returns to clinical latency, (b) warning hemorrhages, accompanying an exacerbation of a pulmonary tuberculosis of variable gravity. 2. Rare hemorrhages, occurring in the course of a confirmed ulcerative tuberculosis, (a), with exacerbation, (b) without exacerbation. 3. Recurrent hemorrhages, (a) cases of hemorrhage at long intervals, (1) without exacerbation, (2) with exacerbation of attenuated pulmonary lesions, (b) erethic forms of fibrocaseous tuberculosis. 4. Hemorrhages of galloping consumption. 5. Final hemorrhages of cavity cases. As to the immediate cause of hemorrhage, pulmonary hypertension seems to be far more important than general high arterial pressure. In 270 autopsies made by Boucicaut and Letulle, 84 hearts were found atrophied, 71 normal, and 115 hypertrophied. The atrophied hearts were found especially in cachectic subjects, in the young, and in cases of intestinal tuberculosis; the hypertrophic hearts were associated with fibrous tuberculosis, emphysema, pulmonary sclerosis, pleural synechia,—conditions which increase the pressure in the pulmonary artery. Superalimentation is an occasional cause.—*Formes cliniques, pathogénie et traitment des hémoptysies tuberculeuses, F. Bezançon and S. I. de Jong, Rev. d. l. tuberc., 1921, ii, 1.*

Case of Gastric Tuberculosis.—A female patient had severe pain half an hour after meals and at night. Chemical gastric analysis revealed an absence of hydrochloric acid and occult blood, and the presence of lactic acid. Roentgenologically, there were extensive changes at the greater curvature and at the pylorus. A diagnosis of acute gastric or duodenal ulcer was made. Operation revealed a typical tuberculous ulcer involving only the mucosa. After transverse resection the patient gained in weight and was without complaints for three months. Then belching, vomiting and nausea set in. At a second operation extensive adhesions were found at the pylorus and a posterior gastroenterostomy was performed to relieve the stenosis. Complete healing of the operative wound was, however, complicated by an exacerbation of the pulmonary process.—*Beitrag zur Magentuberkulose, W. Baetzner, Berl. klin. Wchnschr., December 27, 1920, lvii, 1237.*

Inguinal Lymph Node Involvement in Intraäbdominal Tuberculosis.—In obscure diseases of the abdominal cavity the extirpation of enlarged inguinal nodes for histological examination is justified in the absence of tuberculous affection of the lower extremities or external genitalia. In two cases of tuberculous peritonitis, tubercles were found postmortem in these nodes. In a specimen obtained by biopsy in which there was a considerable enlargement of the nodes and a nodular tumor above Poupart's ligament, extensive caseation and tubercle bacilli were found. The involvement of the lymph nodes is brought about by a reversal in the lymph flow occasioned by caseation in the retroperitoneal nodes. by extension from the anterior abdominal wall, and by anastomosis between the abdominal and pelvic vessels. Conclusions must be cautiously drawn in leukemic or pseudoleukemic cases.—*Einige Erfahrungen über tuberkulose Erkrankung der Leistendrüsen bei intraäbdominaler Tuberkulose und die*

Möglichkeit ihrer Verwendung zu diagnostischen Zwecken, E. Mathias, Berl. klin. Wchnschr., January 17, 1921, lviii, 52.

Pedunculated Tuberculosis of the Peritoneum.—A case of pendulous tuberculosis of the peritoneum is reported, preceded by a brief review of the only other two cases of human pedunculated peritoneal tuberculosis recorded in the literature. The condition is compared to the lesion in tuberculosis of the serous membranes of cattle designated as *Perlsucht*, with which it is pathologically identical. An attempt is made to associate with the process the bovine type of tubercle bacillus and there follows a discussion of the relative virulence and importance of the bovine and human types of tubercle bacilli in different forms of human tuberculosis, together with a brief review of the methods for differentiation of the two types of bacilli. The pathology is discussed from the standpoint of representing the intestinal equivalent of the multiple benign sarcoid of the skin, in reality low grade tuberculous infections, better termed nodular cutaneous tuberculomas.—*Pedunculated Tuberculosis of the Peritoneum: Perlsucht: Extreme Infrequency of the Condition in the Human: Report of a Case with Discussion of Bovine Infection, H. M. Ray, Am. J. M. Sc., clxii, 237.*

Development of Renal Tuberculosis.—The kidney is never the primary location of a tuberculous invasion. It always represents an infection that has been transferred from some other focus in the body. The theory that the tuberculous infection is carried to the kidney from the thorax by way of the lymphatics is not satisfying. It offers no adequate explanation for those cases in which the process is apparently secondary to a tuberculous bone or joint lesion. Evidence is against the probability that the infection in renal tuberculosis ascends from the bladder except in very rare instances. The most satisfactory explanation is to assume that the tubercle bacilli are brought to the kidney by the blood stream. This will account both for the infections having their origin in old tuberculous lesions of the thorax or abdomen and for those that come from an old bone lesion situated some distance away. There are certain objections to this theory. In other hematogenous infections of the kidney the infection is almost always bilateral. In renal tuberculosis the tuberculous lesion is confined to one kidney in most cases. Furthermore, the fact, that once a kidney has been demonstrated to be tuberculous the disease usually progresses until that kidney is destroyed, apparently speaks against the probability of hematogenous infection. From three cases observed and reported, Chute formulates the hypothesis that incipient and very mild degrees of renal tuberculosis are probably more common than recognized. If the hematogenous origin of the infection is accepted, it must be assumed that tubercle bacilli are brought in approximately equal numbers to both kidneys, and that slight cortical tuberculous infections are common and are probably overcome in the majority of instances. The generous blood supply of the kidney probably allows it to overcome the greater number of infections and in only relatively few cases in which one kidney is especially susceptible, possibly due to a local injury, the tuberculous process overpowers the kidney and progresses to the point where it is recognizable through pus in the urine. When the process reaches this stage it is quite advanced and ordinarily incapable of cure. In Chute's opinion, some of the patients, who complain of dull pain in the loin and who present a sterile pus with a few blood cells and leucocytes, are carrying on a struggle to determine whether a tuberculous infection shall overcome a slightly infected kidney or whether the kidney will be able to stamp out the infection. This has a practical bearing and it should be insisted that a patient having occasional attacks of acute pain or constant dull pain in one loin, with a urine showing a little blood and leucocytes, should be urged of the importance of rest and the building up of his resistance.—*Some Hypotheses Regarding Renal Tuberculosis, A. L. Chute, Jour. Urol., May, 1921, v, 431.*

The Laboratory Diagnosis of Renal Tuberculosis.—The following topics are discussed in considerable detail: Gross and microscopic findings of the urine in renal tuberculosis; bacteriology of the urine in renal tuberculosis; tubercle bacilluria; comparative value of the smear and inoculation methods; excretory tuberculosis; rôle of genital, tuberculosis, as a possible source of error, in the diagnosis of renal tuberculosis; and diagnosis of bilateral renal involvement and its influence on operation.—*Cultures, Smears and Guinea Pig Inoculations in Diagnosis of Renal Tuberculosis: their Value and Reliability, A. Hyman and L. T. Mann, J. Am. M. Ass., September 24, 1921, lxxvii, 1012.*

Rationale of Diagnostic Catheterization in Tuberculous Kidney.—*Conclusions:* 1. In renal tuberculosis, catheterization of the sound kidney preliminary to extirpation of the other diseased kidney is not without danger, and can bring about an insidious infection of the second kidney. 2. The positive finding of tubercle bacilli in the catheterized urine of the remaining kidney is not positive evidence of tuberculosis of this organ, for the bacilli can have been introduced from the bladder by the ureteral catheter and thereby artifically mixed. Such a positive finding should not be considered a contraindication to operation on the diseased side. 3. As a diagnostic point preliminary to operation, it suffices that it be definitely established that the remaining kidney is functioning (determined by indigo carmine chromocystoscopy). 4. Bilateral ureteral catheterization in renal tuberculosis is used only as a last resort in those exceptional cases in which chromocystoscopy offers no definite result. It can be considered free from danger only in those early cases which are without involvement of the bladder. 5. in proved bilateral disease it is proper to remove the badly injured pyonephrotic side which is sapping the strength of the patient by pus formation and by giving rise to ulcers of the bladder, thereby increasing the excruciating pain. A definite point in deciding upon removal is the ability of the second kidney to excrete indigo carmine to a certain degree. These conclusions are preceded by a discussion of the literature, the various opinions which have been held upon the subject and a brief summary of various experimental evidence. The points made are illustrated by case histories.—*Muss und darf man vor Extirpation einer tuberkulosen Niere zurucklassende Niere katheterisieren? E. Joseph and N. Kleiber, Münch. med. Wchnschr., January 21, 1921, lxviii, 61.*

Unusual Forms of Tuberculosis of the Joints.—In two cases of tuberculous joints there occurred a purulent synovitis not occasioned by mixed infection nor associated with caseation. The first case manifested itself clinically as an osteomyelitis with ossifying periostitis of acute pyogenic type. The pus consisted of polymorphonuclear leucocytes and was microscopically free from tubercle bacilli or other bacteria. Inoculation tests were also negative. An exploratory excision of suspected sequestra revealed tubercles. In the second case the pus consisted of lymphocytes and polymorphonuclear leucocytes; tubercle bacilli were found. The allergic hypersensitiveness occurring in the second stage of phthisis and causing exudative processes is looked upon as an explanation for the above joint affections.—*Über besondere Formen eitriger Gelenktuberkulose. E. Melchior, Berl. klin. Wchnschr., June 13, 1921, lviii, 634.*

Differential Diagnosis of Early Tuberculous Joints.—Emphasis is laid upon the fact that obscure joint disease which responds favorably, both subjectively and objectively to hot air treatment, is usually nontuberculous in origin. Tuberculous joints, on the other hand, show no improvement when so treated.—*Zur Differentialdiagnose bei beginnenden tuberkulosen Gelenkerkrankungen, J. Oehler, Münch. med. Wchnschr., July 16, 1920, lxvii, 845.*

The Skin as an Organ of Internal Secretion.—The skin possesses more important properties than that of excretion and mechanical protection. It may produce certain substances that are necessary for basal metabolism or substances that are able to detroy toxins. There is an intimate relationship between the epithelial surface of the malpighian layer and the capillary circulation and the nerve supply and lymph spaces. It is conceivable that the skin can elaborate a secretion similar to that of the thyroid, suprarenals, etc., although this cannot be proved. There is evidence of an intimate connection between the glands of internal secretion and the skin, as is seen by the appearance of myxedema with the loss of thyroid function, the dependence of certain skin eruptions or pigmentation on the sexual glands, pregnancy, puberty, and the menopause; also the appearance of the discoloration of the skin in Addison's disease. Furthermore, in many infectious diseases such as measles, diphtheria, smallpox, spotted fever and syphilis, there is a conspicuous involvement of the skin which can probably indicate that the skin performs an important function of overcoming these infections. A popular conception has been that the rash of measles and scarlet fever must be well developed to prevent a serious involvement of the inner organs. A well marked secondary and tertiary involvement of the skin in syphilis often safeguards against later involvement of the nervous system in this disease. All this may justify the assumption of a protective function biologically in the skin; and the value of sun baths and ultraviolet radiation in treatment of tuberculosis may be found in the stimulation of the skin to the production of an internal secretion.—*Internal Secretions of the Skin, K. H. Doege, Wisconsin Med. Jour., August, 1921, xx, 125.*

Ozena and Tuberculosis.—The question of the etiology of ozena has not been settled, but that the disease is very frequently associated with tuberculosis is an undoubted fact. This should cause physicians to carefully examine patients with ozena for possible signs of tuberculosis. Out of 28 collected cases of ozena that have come to autopsy, tuberculosis was the cause of death in 15. A family history of tuberculosis was found in 73 cases out of 129 cases of ozena. Definite clinical tuberculosis was discovered in 52 out of 126 cases. Of the various remedies that have been tried in the treatment of ozena, by far the best results have been obtained with the use of tuberculin. Whether the amelioration of symptoms following the use of tuberculin is due to a general tonic action or is the result of the introduction of a foreign protein into the blood or whether there is some direct action on the nasal disease is not known. The fact remains that there is a cessation of the nasal discharge and an improved condition of the general health following treatment with tuberculin.—*Ozena and Its Relation to Tuberculosis, F. H. Linthicum, Am. J. M. Sci., August, 1921, clxii, 216.*

Bronchopulmonary Spirochetosis.—This disease usually commences as an acute bronchitis with bloodstained sputum. In a few days the acute symptoms pass off and the patient may make a comfortable recovery. More usually, however, a chronic bronchitis ensues, with loss of weight, emaciation and chronic cough. This is accompanied by attacks of hemoptysis, which may be copious but are more frequently slight. The sputum is abundant, frothy, and varying in color from faint pink to bright red. These hemorrhages somtimes last for weeks and then may stop for weeks. In the acute stage, the sputum is always swarming with spirochetes. In the chronic form spirochetes are often absent for considerable periods. In one of the author's cases they were first discovered in the eighteenth specimen of bloodstained sputum examined. The organisms are large and polymorphous, with from two to nine spirals. They are said to be motile. The author's specimens showed up well with congo red. Carbol-gentian violet is also recommended as a stain. As practically all cases of spirochetosis are diagnosed as pulmonary tuberculosis, it would be well if all bloodstained sputa negative to tubercle bacilli were examined for spirochetes. Farah, in the *Lancet*, October, 1919, records that of 22 cases of hemoptysis examined at Beirut, 12 had tubercle bacilli and 6 spirochetes. The disease while usually found in the tropics is also occasionally found in patients who have never been there. Apparently nothing is known of the mode of infection or of the life history of the spirochete. Treatment is unsatisfactory.—*Broncho-Pulmonary Spirochaetosis, C. J. C. Faill, Tubercle, June, 1921, ii, 401.*

The Pathology and Treatment of Empyema Complicating Pulmonary Tuberculosis.—All surgical treatment of this condition must aim at complete expansion of the lung, as otherwise a dead space, particularly susceptible to infection, will be left. However, the laws for the treatment of the underlying tuberculosis of the lung demand that this organ shall not be allowed to reëxpand rapidly, as spread of disease will surely follow. Therefore, drainage by a simple thoracotomy is contraindicated. Empyema accompanying pulmonary tuberculosis may be of several different origins. After collapse of the lung by artificial pneumothorax, the pleura may show a true tuberculous involvement; or because of the mechanical disturbance fluid may form within the large cavity left by the compressed lung. In the former case the exudate is very frequently purulent and due to the unaided tubercle bacillus. So long as this exudate does not exert sufficient pressure on the mediastinum it can be left alone, but if too much displacement occurs death will follow. Or again, an *empyema necessitas* may follow in the form of a subcutaneous, subdiaphragmatic or intramediastinal abscess connected with the intrapleural cavity by a fistula. Sometimes perforation into the lung may occur through the thin pleura overlying a cavity. Such a rupture will be followed by evacuation into the cavity, and the exudate will be coughed up. The clinical picture is very characteristic. After a severe sudden strain, there is intense pain on the affected side, and the patient goes into a state of collapse. The beathing is short and jerky, the pulse is small and feeble, and the temperature rises on the following day. There is a sudden copious purulent expectoration which contains relatively few tubercle bacilli. The patient's condition rapidly becomes worse and he finally dies of sepsis or of amyloid disease. Exploratory pleural puncture yields streptococci or pneumococci. On the other hand, intrapulmonary cavities may rupture into the pleura. In such a case there is a sudden decrease in the amount of expectoration, which will be resumed only when the fluid in the pleura has accumulated to the level of the point of rupture. The clinical course is very similar. The fact that the empyema is in communication with a bronchus may be proved by the injection of 1 cc. of methylene blue into the pleural cavity, when the sputum will be colored blue. A third type of empyema has been very common since the introduction of therapeutic pneumothorax. The pleura is most sensitive to any irritation and moreover there is a natural tendency for fluid to collect within any empty cavity within the body. It is not strange, therefore, that exudates collect in the cavity produced by this form of treatment. The fluid may remain sterile and as long as no undue pressure on the mediastinum is exerted all is well; or infection of the fluid may occur. The latter event is only very rarely due to an infected needle, but is usually from within, either because of torn adhesions or by direct lymphatic extension through the scar tissue of the pleura, or the bacteria may be transported by the blood from remote sources, such as furuncles, osteomyelitis, etc. As they find a point of lessened resistance in the traumatized pleura they there set up a focus of growth. Occasionally a spontaneous rupture of the lung into the pleura may occur, to be followed by a more or less severe empyema. As such cases are already weakened by a severe constitutional disease, a radical operation like thoracotomy is only to be thought of as a last resort. In surgical treatment the chief aim should be to avoid the establishment of a permanent communication between the pleura and the exterior. Thoracentesis is indicated when a serous effusion causes undue pressure upon the mediastinum. Such withdrawals must frequently be repeated and often they become purulent later. If such fluids are infected with tubercle bacilli this procedure is especially deleterious, as the manipulation will only increase the severity of the infection. In such cases some method for disinfecting the fluid (Lugol's solution) should be employed. If a mixed infection is present only thoracotomy remains. Resection of ribs and the employment of an extrapleural Mikulicz tampon without protracted drainage are recommended. This allows evacuation of the pus, continues compression of the lung, and leaves no dead space in communication with the exterior in which further pus can accumulate. The results are favorable. If fistulae persist they may be closed later by a plastic operation. Spengler's treatment consists in aspirating the pleural cavity and then, by an extrapleural thoracoplasty, compressing the cavity and thereby limiting the space within which new exudate may collect. Friedreich's operation of paravertebral rib resections done at several sittings should also be preceded by a thoracentesis. For sterile, slightly purulent exudates, or those containing tubercle bacilli only, thoracentesis, followed by replacement with nitrogen, should be tried first. These failing, thoracoplasty in several sittings is recommended. This is absolutely necessary where apical adhesions prevent the collapse of intrapulmonary cavities. The mortality is high but in a limited number of cases the operation has been successful.—*Die Behandlung der tuberkulosen Pleuraempyeme, W. Jehn, Münch. med. Wchnschr., May 6, 1921, lxviii, 537.*

Climate and Weight in Tuberculosis.—In 1914, Strandgaard, of Boserup Sanatorium, Denmark, pointed out that certain variations took place in the average weekly gains in weight of patients in the Sanatorium. He attributed these variations to the influence of the climate. This led in 1917 to similar investigations being made in Finland and the results corroborated those obtained in Denmark. In 1920, investigations in England showed the bad effect of strong, prevalent, rain-bearing winds on the course of tuberculosis. All this evidence made clear the importance of careful choice in the selection of sites for sanatoriums. The author was called upon to make similar investigations in South India and found that at the sanatorium in Arogyavaram the patients' weekly gains in weight varied as they did in the sanatoriums in Northern Europe. In South India the curve showing the weekly gains in weight in the different months of the year has a form nearly opposite to that in Northern Europe, as it shows the minimum gain in weight in the summer, while in Northern Europe the minumum occurs in the winter. In South India, as contrasted with Europe, the heat and sunshine are detrimental to the gain in weight. It seems, therefore, that meteorological conditions have a great influence on variations of gains in weight. Humidity seems, as in Northern Europe, to be a beneficial and necessary condition for the greatest increase in weight, although in South India a heavy rainfall produces a transient decrease. In South India, as in Northern Europe, the variations in the humidity of the air have probably the greatest influence on the weekly variations in gains, while the heat seems to be the deciding factor of monthly variations. In South India the site for a sanatorium should not be on the plains with the very hot climate, or in those parts of the country where the rainfall is chiefly brought about by heavy monsoon storms. Nor should the site for a sanatorium be selected in a place with too dry air. The best location seems to be in an up-country locality, not too high above sea level, securing a cooler and moderately moist climate with a mild, refreshing breeze.—*Climate and Weight of Tuberculous Patients in South India, C. Frimodt-Möller, Tubercle, June, 1921, ii, 385.*

Artificial Pneumothorax Therapy.—Saugman in the *Lancet* (1920, ii, p. 685) showed that 38.5 per cent of the patients who had undergone pneumothorax treatment were fit for work in from two to twelve years after discharge, whereas this was the case with only 11.8 per cent of those whose pleural adhesions prevented the adoption of this treatment. The difference between these two groups would have been still greater had not the first included several cases with partial pleura adhesions. The importance of these partial adhesions has not before been expressed in figures, and the author, who is first assistant to Saugman at the Vejlefjord Sanatorium, has prepared a table with the view of throwing light on this point. This table shows that of the cases in which a pneumothorax could be induced, about 35 per cent (20 per cent of the total material) failed to show appreciable adhesions on searching examination. In 70 per cent of these cases, the patients were fit for work after an observation period of from three to thirteen years. In the remaining cases there were some in which the adhesions were confined to strictly limited areas, and the pneumothorax was in other respects complete; in these the percentage of cures was about 33 per cent. In other cases in which adhesions were comparatively extensive, and the pneumothorax was small, the percentage of cures was only about 11 per cent. These figures show the sinister importance of adhesions. Among the first 60 cases selected for operation at the Sanatorium, 6 died. Of the surviving 54 cases, 7 achieved relative recovery, that is, they were symptom free and had been fully fit for work for at least a year; in 16 there was marked improvement; 17 were improved; in one there was no noticeable change; 11 became worse and have since died; and 2, after obtaining marked benefit, died of influenza. Thus, in 42 cases a positive result and in 18 a negative result were obtained. All the cases were sputum-positive before the operation, and 31 became negative. Persistent hemoptysis in 2 cases was arrested by the operation. Before the operation 25 cases were febrile; of these 14 became afebrile. It is important to note that the operation in every case was carried out in the Sanatorium.—*Lung Collapse Therapy in Connection with Pleural Adhesions, J. Gravesen, Tubercle, June, 1921, ii, 395.*

A Complication of Artificial Pneumothorax.—Why a patient with a pleural effusion of tuberculous origin on one side is usually immune to pleurisy with effusion on the other cannot be explained. The same is true of therapeutic pneumothorax whether or not complicated by hydropneumothorax. Because of the extreme rarity of this complication the author reports a case, only two others having been observed, of an effusion with multiple fluid levels on the side treated and with pneumothorax and another effusion on the untreated side. It is noteworthy that in all three cases the artificial pneumothorax was induced on the right side and that the first effusion occurred on the side of the pneumothorax. It would be expected that with one lung completely collapsed by a pneumothorax and the other compressed by a pleural effusion the danger of respiratory embarrassment would be immense, but, as a matter of fact, dyspnea and cyanosis were not the outstanding symptoms in any of the cases.—*Therapeutic Pneumothorax Complicated by Hydropneumothorax and Pleurisy, with Effusion on the Untreated Side. Report of a Case, B. P. Stivelman, Am. J. M. Sci., clxii, 270.*

Heliotherapy in Laryngeal Tuberculosis.—Seven cases were treated with lowland sunlight. Four showed marked improvement while three were uninfluenced. However, the latter were unable to carry out the treatment properly on account of advanced illness. Of those considerably improved, two had extensive ulceration as well as extensive disease of the lungs. All patients had active pulmonary disease.—*Laryngeal Tuberculosis with Special Reference to Sunlight Treatment, F. B. Stafford, Virg. Med. Monthly, August, 1921, xlviii, 239.*

A Formula for Light Treatment.—Just as in the employment of drugs, so here it is essential to determine exact dosage. As a means of accomplishing this the author has constructed his formula, called a *Nomagram.* Intensity of light effect increases proportionately with the period of raying, and decreases proportionately inversely with the square of the distance. The presence of lenses, reflectors and additional sidelights must be considered also. $M = Z^2 : E^2$ in which M is the number of units employed, Z the minutes of exposure and E the distance in centimetres. The construction of the scale which has been worked out rests upon logarithmic principles.—*Ein Nomagramm für die Lichttherapie, L. Zimmermann, Münch. med. Wchnschr., August, 1920, no. 35, 1019.*

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Abstracts should be sent typewritten on one side of the page only. They should be as concise and compact as the subject matter of the article warrants. They should be headed with a short title, and followed by the full title of the paper, author's name, journal, date, volume and page.

The Heart in Early Pulmonary Tuberculosis.—In examining a patient for possible phthisis the writer points to the value of the heart examination. The pulmonary second sound in the absence of any organic right ventricular hypertrophy is usually accentuated in early phthisis. The heart of the consumptive is small. Hypertrophied hearts are exceedingly rare in phthisis. If the heart is of normal size in incipient phthisis, it is believed to share in the general cachexia as the disease advances. It has been shown that in proved tuberculosis, with bacilli in the sputum, the accentuation of the pulmonary second sound persists even though percussion of the right heart, X-ray plates and fluoroscopy fail to show any right ventricle hypertrophy. Therefore, when a patient presents himself for examination, and among other findings his pulmonary second sound shows a definite accentuation without cardiac enlargement, it is well to bear in mind the possibility of phthisis.—*A Sign of Value in Early Phthisis, S. Simon, J. Missouri State M. Ass., January, 1921, xviii, 11.*

Importance of Exact Measurement of Intrapleural Pressure in Artificial Pneumothorax.—The author stresses, not the pressure on initiation of pneumothorax, but its record in the course of treatment, for its bearing on processes taking place in the pleural cavity, such as tension on adhesions and displacement of the mediastinum. He uses as his measure of pressure the difference in level of the liquid columns in the two large bottles of the usual apparatus, at the point where no more gas will enter the cavity. His manometer is thus of such calibre, 6 cm. or more, that oscillations are negligible; it records accurately the weight pressing on a given area of lung. This method is compared with the popular one of taking the mean between the respiratory excursions in the small bore manometer; figures are given indicating that the latter method is inaccurate. The injection is made gradually by lifting the bottle from which pressure is derived 1 cm. at a time. This method is slow, but possesses a measure of safety by virtue of that fact. Two absolute requirements for the correct measurement of pressure are a needle, 0.8 to 1 mm. inside diameter, and cotton filters permitting the passage of 600 cc. of gas in from fifteen to twenty seconds. Curves are kept during the process of filling, in which volumes are plotted on the abscissae and pressures on the ordinates. That for a normally collapsing lung is a straight line inclining at about 45 degrees. Variations from this indicate a variety of untoward developments, described in detail with figures in the text. The practice of making curves during the injection is thus

a measure of diagnostic importance.—*Importance des measures exactes de la pression pleurale dans le traitement de la tuberculose pulmonaire par le pneumothorax artificiel (I), G. Küss, Rev. d. l. tuberc., June, 1921, 3rd series, ii, 163.*

Recovery of Respiratory Capacity after Artificial Pneumothorax.—By means of a Chauveau spirometer, adapted for nasal breathing, the volume of air respired after total or partial pneumothorax was measured from day to day in patients at the Sanatorium F. Mangini at Hauteville. Along with the respiratory capacity, in both normal and forced breathing, the rate and the intrapleural pressure were observed. The data, represented as curves, are so superimposed as to show for a patient, at any given time, his respiratory capacity and frequency and the intrapleural pressure. The rapid fall in respiratory capacity that follows the collapse of a lung may equal a fourth of the total capacity before pneumothorax. If the collapse is progressive the fall is less, since compensation is established gradually; the volume measurements, therefore, agree with the clinical experience that less discomfort accompanies the gradual induction of a total pneumothorax. Compensation, produced by increased frequency and greater expansion, is established more easily in young than in older persons, and, perhaps, more easily in men than in women. The total respiratory capacity cannot only be regained, but is even increased. When the normal frequency is reëstablished, the respiratory capacity in normal breathing is greater than it was before the pneumothorax. The frequency, which rises almost at once to its maximum, decreases gradually as capacity increases, but it does not reach normal until after the latter has been fixed for some time at a point above its initial value. These results agree with laboratory findings which show that penumothorax increases pulmonary exchange. Recuperation may be very rapid (fourteen days) or it may be slow; various factors are concerned, such as the formation of the chest, the state of the active lung, age, health, etc. But, in general, the respiratory capacity, after its great initial fall, increases at first very rapidly; then more slowly to its maximum. Forced respiration or capacity after a pneumothorax does not follow so regular a curve as normal respiratory capacity or respiratory frequency. The volume due to forced respiration falls rapidly after total pneumothorax and less rapidly after partial pneumothorax. Recovery of forced respiratory capacity is always slow. It is more rapid in early than in late life, but in the most favorable cases it never takes place as quickly as the return of normal respiratory capacity. This agrees with the clinical experience that persons with a pneumothorax need considerable time to regain a normal capacity for physical work.—*Recherches expérimentales sur la récupération de la capacité respiratoire chez les sujets traités par le pneumothorax artificiel, F. Dumarest and J. Delong, Rev. d. l. tuberc., 1921, ii, 99.*

Phototherapy of Ocular Tuberculosis.—Many workers have tried to measure the intensity of light derived from quartz lamps; some by biological methods, and others with dye reactions, layers of silver, colloidal solutions and selenium cells. It is necessary to remember that healthy tissues will absorb light differently from diseased tissues. Lamps will vary in their intensity in accordance with the life of the burner. To affect the deeper tissues, fluorescent substances can be used which change the short waves into long waves, or sensitizing substances which give to the long waves the chemical properties of short waves. On the eyes of rabbits Passow showed that after decreasing the distance between the lamp and the eye there was a uniform increase of the inflammation. With small doses one could obtain an inflammation and with large doses a necrosis. The voltage and amperage of the current and the period of raying, the distance, the age of the lamp and the type of lamp must all be measured. The author employed a Bach quartz lamp of 110 volts which had been used for one hundred to two hundred hours. After universal radiation employed in all forms of scrofula of the eye, the prognosis is best in children. The entire body is rayed every other day at a distance of 60 cm., beginning with five minutes, then ten, and after that fifteen minutes front and back. The eyes are only slightly closed. One hundred children were observed for over two years. In one-half of the children one to three rayings gave excellent results, and in the other half, four to six. Infiltrations were absorbed and ulcers healed. Rapid disappearance of the swelling and catarrhal discharge were noted. The eczema of the face was markedly bettered. In almost all cases the result was good. The younger the child and the shorter the disease, the better were the results. An indirect hematogenous action is probable. Similar favorable results by this method of treatment have been reported by Seefelder, Koppe, Augstein and Axmann. Indications for local raying are lupus of the lid, keratitis, tuberculous episcleritis, macula of the cornea, iritis and tuberculous iridocyclitis, choroidoretinitis and tuberculous periphlebitis. In lupus of the lid the results are good when the eyes are rayed without protection but with the lids closed, and with the same doses as with general raying. In diseases of the cornea such as opacities, infiltrations and ulcers, the eye is rayed at a distance of from 60 to 100 cm., depending upon the stage of irritation of the eye. The duration of the first raying is always five minutes. The following lengths of exposure are determined by the reaction of the diseased tissues, but the period is generally ten minutes for the second dose. In general, one can usually rely on a raying of five minutes at a distance of 80 cm. as safe, and yet therapeutically helpful. With the left hand the lids are opened and with the right is held a large round shield containing an opening the size of the cornea, so that only the diseased area is rayed. If there is not too strong an irritation, no pain occurs. Animal experiments with a similar lamp on rabbits showed that at a distance of 40 cm. and with five minutes' exposure, ulceration of the cornea resulted. At 50 cm. and five to ten minutes raying, there were only epithelial changes which soon disappeared. At 60 cm. no harm resulted. Harm to the inner eye can be disregarded. Results in nodular types of opacity, corneal ulcerations and infiltrations of a probable tuberculous origin were best. Generally, after two or three exposures there was an increased hyperemia in the diseased area and a slight injection around it. Raying was resumed when the previous injection had disappeared. In disease of the inner eye results are not so promising. One cannot expect positive results in diseases of the iris and ciliary body. To protect the cornea from the action of large doses for inner eye disease, one can place a uviol glass or even ordinary window glass between the light and the eye. This will keep out the short ultraviolets and increase the amount of light. The lens absorbs the short rays from $310\ \mu\mu$ down and in many cases up to $375\ \mu\mu$. The longer rays probably reach to the retina. Koppe claims that he has healed many cases of tuberculosis of the inner eye by general radiation. It may also be true that with the proper fluorescence or sensitizing substances, the inner eye can be likewise affected by direct radiation. Finally, X-ray and radium on account of their harmful effects on the eye cannot be employed for tuberculous diseases of this organ.—*Beitrag zur Bewertung und praktischen Anwendung der Lichtbehandlung bei tuberkulösen Augenerkrankungen, A. Passow, Strahlentherapie, April 20, 1921, xii, 441.*

Results of Treatment of Lupus Vulgaris and Surgical Tuberculosis with Artificial Chemical Light Baths.—Reyn is opposed to the theory that the stronger the pigment the better the healing effect. With a carbon arc light he aims to obtain a marked erythema without pigmentation. The carbon arc is used for general radiations together with additional local exposures. The Finsen light gives much better results (up to ninety per cent) than raying with the quartz mercury light, but even here hundreds of radiations over prolonged periods are necessary. Ernst reports excellent success with light radiation in all forms of surgical tuberculosis, offering statistics to show better results with the carbon arc light than with the mercury quartz light.—*Die Resultate der Behandlung mit künstlichen chemische Lichtbadern bei Lupus Vulgaris und chirurgischer Tuberkulose, A. Reyn and N. Ernst, Strahlentherapie, January, 1920, x, 314.*

The Light Treatment of Venereal Diseases.—The bactericidal destroying properties of light play only a small part in the destruction of diseased tissues. The circulatory changes are much more important. It is essential that general applications of light should be made in addition to local ones. For local applications we must always radiate some healthy skin around the diseased area. There is evidence that the skin, as a protective organ, throws off antibodies. When one-third of the skin has been destroyed by severe burns, death results. Diseases like measles, scarlet fever, smallpox, typhus fever and syphilis, in which rashes appear, almost always confer an immunity after one attack. Trichophyton has been shown by Bloch to confer a distant healing action on other parts of the body when pieces of skin are injected or later transplanted. Protective antibodies are formed which produce this distant action. Inoculation of the skin with cowpox can protect against smallpox. Intracutaneous treatment seems to be more valuable in many cases than the subcutaneous treatment. In syphilis severe skin rashes are seen only in those cases that do not develop tertiary lesions later. If severe skin infection develops in the third stage of syphilis, then the inner organs generally remain free. Local radiation of furuncles may heal the infection but general radiations are necessary to prevent metastatic recurrences. Treatment for nearly twenty years has convinced the author of the great value of light radiations in the treatment of syphilis, with general radiations employed in any stage. Local exposures are also given when indicated. Gonorrhea has also been treated with satisfactory results. Slight redness is the desired effect on the skin. Twenty minutes is the longest period of exposure employed. The specific treatment of syphilis is, of course, carried on in addition to the light exposures.—*Lichtbehandlung bei Geschlechtskrankheiten, nach 20 jahriger Erfahrung, S. Breiger, Münch. med. Wchnschr., August, 1920, no. 35, 1012.*

Light in the Treatment of Syphilis.—Syphilis in the tropics, although widespread, is generally of a milder character and tabes and paralyses are seldom seen. Under the action of light there is an increase of cells in the cutaneous basal layer and a hastening and strengthening of the cornification process. Under the action of light the skin assumes a series of properties that are most important for health. Inner secretions are given off by the skin; so that in this way light indirectly affects the diseased areas. The skin is richer in cells, gets better circulation, has better respiration and excretion, and regulates warmth and protects better. Syphilis, like tuberculosis, affects the skin and subcutaneous tissue, the lymph nodes, the inner organs and the nervous system. It has been noted that in patients with tabes and paralysis there was generally a failure of strong skin reactions, and those with strong general reactions and skin rashes very seldom developed tabes and paralysis. The patients treated by the author in no instance developed tabes and paralysis. Three patients who had been treated with sunlight, after three, five and eight years developed reinfections. Of course the light was used only as an aid to the mercury and salvarsan treatments.—*Die Rolle des Lichtes in der Luestherapie, E. Hesse, Strahlentherapie, April 20, 1921, xii, 461.*

Exposure of the Cornea to Ultraviolet Light.—Birch-Hirschfeld, after prolonged observations on animals undergoing exposure of the eye to ultraviolet rays, noted severe damage not only to the conjunctiva and cornea but also to the iris and retina. Since he applied rather large doses it seemed desirable to repeat the work. The author employed a Kromayer lamp in cylindrical form, so as to localize the rays over a small area of the cornea. The period was five to fifteen minutes. After a few hours there was a marked irritation of the conjunctiva, which gradually increased and after one and a half to two days gave a rawness to the superficial part of the cornea which was clearly demarcated from the normal tissue. The corneal clouding gradually receded to normal and on the fifteenth day had entirely cleared. No other inflammatory changes were evident in the eye. Microscopic examinations of the iris and lens, retina and ciliary bodies showed no changes. In another series of experiments in which the cornea was rayed for one hour, no irreparable damage was done. After fourteen days it was entirely clear. Therefore, in sluggish forms of keratitis there is no danger in using the light and good results are obtained. The painful irritation phenomena are best stopped with a 2 per cent cocaine salve and moist bandages soaked with trigeminon or pyramidon.—*Experimentelle und klinische Beiträge zur Bestrahlung der Kornea mit ultraviolettem Licht, T. Chotzen and E. Kuznitsky, Klin. Bl. f. Augenheilk, 1919, xl, 198.*

Ultraviolet Light Treatment of Heart and Vascular Diseases.—Ultraviolet rays lower blood pressure. Excellent reesults are obtained by a combination of quartz light raying and mineral baths. Irregularities, intermittencies and all nervous symptoms disappear quickly. The pulse is more regular, and softer and slower. Blood pressure is lowered and the patient sleeps better and feels better; diuresis is produced. Dilatation of the skin vessels offers less work for the heart.—*Ultraviolettbestrahlungen als neue Grundlage der Therapie von Herz- und Gefässkrankheiten, Schäcker, Strahlentherapie, April 20, 1921, xii, 456.*

Sterilization of the Throats of Diphtheria Carriers with Ultraviolet Rays.—Over forty chronic nose and throat diphtheria carriers were treated by ultraviolet radiation with the Kromayer lamp. All parts of the tonsil are exposed directly for from three to five minutes, so that but one to three applications are necessary to completely cover each tonsil. The rays are applied through a hollow metal tube, one-half inch by six inches long, and so slanted to fit directly over the tonsil. In fifty per cent of the cases one treatment was enough to sterilize, while four cases required three exposures but none required more than that. If the cultures remained positive, the raying was repeated with a four to six minute exposure.—*Sterilization of Nose and Throat Diphtheria Carriers with Ultraviolet Rays, L. C. Donnelly, Michigan State Med. Soc. Jour., July, 1921, xx, 356.*

The Action of Ultraviolet Light on the Inner Organs of Eosin Sensitized Mice.—Eosin employed in amounts of 0.4 gm. per kilo body weight sensitizes mice and rabbits to light exposures. This amount was employed in one per cent solution for white mice. One to two hours after the animals had been injected, they were exposed to ultraviolet radiation for one-half to one hour every day for about five successive days. Autopsies showed dilated vessels and hemorrhages, with round cell infiltration of the liver. Similar changes occurred in the spleen and kidneys, the latter also showing desquamated epithelium. In the lungs the capillaries were dilated and full of blood, while lymphoid cells filled the alveoli. Mice that were killed one and a half hours after injection of eosin showed red discoloration of the kidneys, liver, gall bladder and intestines. The results from about five hours of raying, in combination with eosin, were similar to those that were obtained by sixteen to eighteen hours of raying without eosin. The subcutaneous injection of eosin without the employment of light produced no changes in the deep organs except discoloration. The action of the rays did not depend upon the amount of injected eosin but upon efficient absorption. More marked changes were noted with daily raying than with raying every other day.—*Die Wirkung des ultravioletten Lichtes auf die inneren Organe mit Eosin sensibilisierter Mäuse*, *R. Gassul*, *Strahlentherapie*, *April*, *1920. x*, *1162.*

X-Ray Treatment of Tuberculosis.—Indications, technique and results are taken up in detail. The action is due to the stimulation of the connective tissue growth. Large amounts of granulation tissue form. Indurated lymph nodes give best promise. Caseous and pus foci are rarely influenced. The tubercle bacillus itself is not influenced by the rays. Weak and feverish patients must first become stronger and afebrile before treatment is given. Amyloid and contracted kidneys are contraindications. In the treatment of lymph nodes of the neck it is necessary to cover the larynx. Tuberculosis of the lymph nodes and the bones of the hands and feet and of the ribs and scapula, especially when the foci are closed, is easily influenced by X-rays. Caseous lymph nodes are best treated surgically at first and then given X-ray treatment. Fistulae should first be freed from necrotic tissue, and cold abscesses should first be punctured and later rayed. Lupus vulgaris should be treated by the Finsen method. Disease of the larger bones and joints is only gradually healed with the X-ray. The treatment has not given good results in disease of the peritoneum, genitourinary tract, uterus, ovaries and the gastrointestinal tract. In pulmonary tuberculosis, only the indurative types when they approach latency or are slowly progressive prove suitable.—*Die Behandlung der Tuberkulose mit Röntgenstrahlen*, *E. Mühlmann*, *Therap. Halbmonatsh.*, *1920*, *ii*, *35.*

X-ray Treatment of Tuberculous Lymph Nodes.—This therapy surpasses sunlight because of its more accurate dosage, greater ease of employment, ability to be used at any time, quicker results and fewer residua. In anemic and weak patients, it is employed in connection with the ultraviolet light. The virulence of tubercle bacilli is diminished. A dose strong enough to kill bacteria is, however, too large and is liable to burn the skin, but the resulting proliferation of connective tissue works against the growth of bacteria. Besides having a local action X-ray treatment also increases general resistance. Secondarily infected nodes are much more difficult to heal.—*Röntgentherapie der tuberkulösen Lymphdrüsen*, *S. Simic*, *Srpski Archiv.*, *1920*, *i*, *33.*

Action of Radium and Roentgen Rays on Normal and Diseased Lymphoid Tissue.—Circulating lymphocytes are most readily influenced by radium and roentgen rays, while the other normal types of leucocytes and red blood cells possess greater resistance. Normal lymphoid tissue is comparatively less sensitive to the rays than the various types of diseased lymphoid tissue. Hodgkin's disease and lymphosarcoma are particularly susceptible to radiation. Myeloid leukemia is especially susceptible to radium and roentgen rays, but myelocytes in conditions other than these are not sensitive. Radiation of the spleen influences considerably the course of various diseases of the blood and lymphoid tissue. In two cases of pernicious anemia it caused a marked shrinkage of the enlarged spleen. The action of the radiation is not merely a local one, but there is a generalized effect on the lymphoid system of the whole body. It may be that specific enzymes are freed from the degenerating lymphocytes. The bone marrow and other depots of diseased tissue may replace the destroyed lymphocytes with the leucocytes. When the animal receives a larger amount of radiation, the total white cell count may go as low as six hundred.—*Action of Radium and Roentgen Rays on Normal and Diseased Lymphoid Tissues*, *I. Levin*, *Jour. Amer. Med. Assoc.*, *September*, *1921*, *lxxvii*, *930.*

Surgical Treatment of Tuberculosis.—König criticizes the conservative methods outlined by Bier in a previous number of this journal. He inquires what these conservative measures have accomplished, that they should be so broadly recommended to the practitioner, and then proceeds to analyze in detail the various surgical conditions and their treatment. In tuberculous cervical adenitis operative interference is to be avoided, if possible, because of the disfiguring scars; treatment by heliotherapy or X-rays is preferable. In certain cases of bone and joint tuberculosis, heliotherapy has undoubtedly given good results, but it very frequently fails. Although comparative statistics of cases treated by operation alone and those handled by conservative measures are wanting, he has collected from the literature 1932 cases of resections for tuberculosis of bones and joints, 68 per cent of which showed permanent healing. The opposition is defied to produce like figures. Extraärticular tuberculous foci in the bones demand operative interference because of the greater certainity of the results, and because less time is required for their cure. In cases of progressive destructive articular lesions resection is imperative. If the practitioner would follow Bier's advice he must experiment upon his patients, and although experiment upon human beings may be necessary, it may be very unfortunate for the patient and should be avoided. He concludes with a plea against slavishly following the conservative advice of Bier and begs that the practitioner make use of operative procedures as these may be indicated.—*F. König.*

Immediately following is a reply by Bier.—He suggests that although a general infirmary is not the place to treat all sorts of tuberculosis, yet if physicians working in such institutions would follow his simple conservative procedures, the patients would be bettered. In reply to König's accusation that he is experimenting upon human beings, he remarks that König is in error, for heliotherapy has demonstrated its worth for twenty years and has passed the experimental stage. He presents no statistics, but states that his cases of "healing" are ones in which a limb is restored to function as opposed to the "healing" after amputation or resection of a joint. Isolated extraärticular foci are rare, and if present do not require resection in his mode of treatment. Often chronic fistulae respond more readily to the light treatment than do the early cases. He concludes by advising all physicians who wish to treat surgical tuberculosis to resort to heliotherapy first.—*Die Behandlung der chirugischen Tuberkulose, F. König, and Bemerkung zu vorstehendem Aufsatz, A. Bier, Münch. med. Wchnschr., May 27, 1921, lxviii, 642.*

Surgical Treatment of Tuberculosis.—Previous to the discovery of the tubercle bacillus, tuberculosis was thought to be a diathesis in which the humors of the body had suffered some disturbance. To correct this disturbance codliver oil and iodine treatments, together with climatic treatment, were in vogue. Surgical treatment was confined to corrective measures applied after the healing of the disease process. Koch's discovery led to attempts at the application of all sorts of antiseptics to the apices of the lungs. Operative removal of tuberculous foci led to rapid dissemination of disease, and the zest for radical operations also led surgeons to disregard the epiphyseal lines, with the result that interference with growth and shortened limbs were frequent occurrences. It followed that the surgery of tuberculosis fell into disrepute. Of fundamental importance in the surgical treatment of this disease is the recognition that it is a generalized disease, the local manifestations of which may call for surgical treatment. General measures have their proper place but are in no sense specific. They probably act by stimulating metabolic activities. Other more specific measures are the injection of iodoform-glycerine and X-ray treatment. The former has no direct germicidal action, but when brought into contact with protein decomposition products it exerts a positive chemotactic influence upon the leucocytes which liberate proteolytic ferments, that break down the hard caseous exudate and promote its absorption. Iodoform-glycerine is useful in the treatment of cold abscesses and fistulae. Depending upon the size of the abscess, from 10 to 30 cc. of a 10 per cent iodoform-glycerine solution is injected, and these injections are repeated at "properly spaced intervals." The X-ray is employed in one-fourth to one-third maximal doses with zinc filters, 0.5 to 0.7 mm. in thickness; the raying is repeated once a month over a period of three or four months. Closed lymph node tuberculosis offers the best type of lesion for this mode of treatment, but marked improvement has been noted in open and closed bone and joint cases, in lesions of the "soft parts", epididymis, and in open lymph node tuberculosis. By combination with sunlight treatment, a further stimulus is added which seems to promote a more rapid fibrosis. The Deycke-Much partial antigens have some value, but the author's experience with them is limited. He has not seen Friedmann's cure employed to the exclusion of other measures, and he has had no experience with tuberculin. Bier's massive hyperemia is probably useful in some joint cases, but it is difficult to judge its value, as it is most often combined with immobilization of affected joints. For this purpose plaster of Paris is preferable to extension apparatus, as children may be sent away for climatic treatment. Joints are rayed with sunlight or the X-rays through windows cut in the plaster. Effusions are treated by the injection of iodoform-glycerine. Isolated tuberculous foci in small bones may be removed without danger. With marked destruction of a joint, resection is indicated. It is a fact that when tuberculosis of an extremity coexists with pulmonary tuberculosis on the same side, amputation of the affected limb will very often cause radical improvement of the lung condition. For tuberculosis of the spine absolute fixation followed by removal of diseased portions is the method of choice. Albee's operation of grafting a portion of the tibia into the spine is useful in some cases. Tuberculous peritonitis should be treated by the above mentioned constitutional methods or occasionally through a laparotomy incision; the peritoneum is swabbed out with tincture of iodine. Resection of a tuberculous cecum will often lead to the spontaneous healing of tuberculous ulcers in other parts of the intestine. If ulceration leads to stenosis, anastomoses are indicated. The use of the X-ray has proved especially valuable in the treatment of tuberculosis of the epididymis. Renal tuberculosis which does not tend to spontaneous healing is treated by excision. An early diagnosis is of great importance. In the surgical treatment of pulmonary tuberculosis artificial pneumothorax is the simplest procedure. The Friedreich thoracotomy, done where extensive pleura adhesions prevented collapse of the lung, gave too great an operative mortality. Sauerbruch's paravertebral resection of the ribs from the eleventh to the first, done in several sittings under local anesthesia, when combined with artificial pneumothorax gives the best results. Wilm's columnar resection gives only a partial compression. Extrapleural pneumolysis, resection of ribs, stripping off the parietal pleura and packing the space with paraffin have likewise been used. Phrenicotomy, to limit the movement of the diaphragm, has been used as an adjunct to these operations. The phrenic nerve can be readily severed in the neck under local anesthesia. Most important of all in surgery of pulmonary tuberculosis is the choice of cases. Only unilateral disease is suitable, and the most favorable cases are those with extensive fibrosis and cavity formation.—*Die Behandlung chirurgischer Tuberkulosen*, *R. Haecker*, *Münch. med. Wchnschr.*, *January 7*, *1921*, *lxviii*, *18.*

Surgery in Pulmonary Tuberculosis.—It is possible by operative procedures to so favorably influence a severe, and particularly a unilateral, pulmonary tuberculosis, that a marked improvement or even complete healing is brought about. Not all cases are suitable for this mode of treatment, however, and such treatment can only be successfully carried out after careful observation by a competent clinician in conjunction with the surgeon. The ideal case for artificial pneumothorax treatment is one in which the disease is confined to an upper lobe which is free from adhesions. Where, because of such adhesions, it becomes impossible to compress the lung by the ordinary method, resection of several ribs and extrapleural compression are recommended. The resections are done in the paravertebral line, allowing compression of the lateral and anterior portions of the thorax. The number of ribs resected must be governed by the extent of the disease. Where the whole lung is covered by adherent pleura, the ribs from the eleventh to the first must be cut, but if there are adhesions over the upper lobe only, the overlying ribs are resected while the lower lobe is compressed by artificial pneumothorax. In cases where the pleura is completely adherent, the lower lobe should always be compressed first, and the upper not touched until a later date, when the lower lobe is completely compressed. The primary mortality from the operation in Sauerbruch's clinic has been 2 per cent. To this is added a delayed mortality of 12 per cent due to fatal progressive involvement of the opposite lung, to aspiration pneumonias, and to faulty selection of cases for operation. It is possible to employ the intrapleural pneumolysis of Jacobaeus in cases where small bandlike adhesions interfere with the compression. This method consists in the inspection of the interior of the pleural cavity by a thorascope and the section of the obstruction by a small electrocautery. Because such adhesions frequently contain vessels which may cause severe hemorrhage or bronchi which may cause infection of the pleural cavity, Sauerbruch opposes its use. If, after attempting to compress the upper lobe by rib resection the lung is still expanded, extrapleural pneumolysis may be tried. This consists in exposing the pleura and tamponing the lung. Frequently, a lung containing a large cavity may be completely collapsed in from eight to ten days by this method. Large, badly infected cavities may be drained through the chest wall at various points, depending upon their location. The resulting lung fistula must be closed at a later date (after two or three months) by a plastic operation. Sauerbruch uses phrenicotomy or section of the phrenic nerve, as a diagnostic rather than a therapeutic measure. The cases reported as cured have been under observation for eight or ten years, and, while not denying that even cavities may heal spontaneously, he feels that his surgical interference has been justified. Up to 1919 he has so treated 381 tuberculous cases, of which 134, or 35 per cent, were "practically healed." Forty per cent were improved. He concludes with a plea for operative treatment alone or combined with artificial pneumothorax, as a means of closing bacilli-laden cavities and thus removing a great source of infection to individuals in the immediate vicinity of the patient.—*Die chirurgische Behandlung der Lungentuberkulose, F. Sauerbruch, Münch. med. Wchnschr., March 4, 1921, lxviii, 261.*

Treatment of Surgical Tuberculosis by the Practitioner.—The increased amount of tuberculosis among the German people since the war has compelled the ordinary practitioner of medicine to treat many cases of surgical tuberculosis himself. Bier recommends that he refrain from attempting to experiment with radical surgical procedures, but that he be content with more conservative measures. In fact, he himself has found operation rarely necessary in such conditions. The chief method of nonoperative treatment is heliotherapy as applied by Bernhard and Rollier. On cloudy days, if the cost is not prohibitive, artificial ultraviolet lamps may be substituted. Bier himself recommends the apparatus of Kisch made by Zeiss. This is of advantage because in addition to the ultraviolet rays it also gives off heat rays and maintains a temperature of about 70°C. Treatment by X-rays is also valuable in lymph node tuberculosis but its use requires considerable technical knowledge. The second method is passive hyperemia, which the unskilled should attempt only on the head and extremities. Bandages (rubber) should be applied with greatest care, and it is of first importance that no pain or discomfort should be experienced by the patient. The third measure is internal medication with sodium iodide, given in daily doses, 3.25 gm. for adults, 1 gm. for adolescents, and 0.5 gm. for children under five years. No ill effects have been observed. This treatment brings about resorption of pus in cold abscesses and of sequestra in bones. Fixation of tuberculous joints should never be practised. Bed rest is quite sufficient for the treatment of tuberculosis of the legs, pelvis and spine; for the upper extremities loose bandaging is employed. Such treatment causes disappearance of pain in a short while and allows sufficient movement of the affected joints. Motion which causes pain should be avoided. Cold abscesses should be aspirated, not with a trocar, but with a small needle. If such aspiration is repeated often enough the abscess will heal without fistula formation. With such methods the ordinary practitioner can successfully treat all cases of lymph node and skin tuberculosis, and all tuberculous lesions of bones and joints which have not advanced to extensive tissue destruction and deformity. The treatment of the last group should be reserved for those skilled in the handling of orthopedic appliances. In his sanatorium at Hohenlychen, Bier treats all classes of cases, many of which have progressed to amyloid changes, and yet by these methods there are 70 per cent of cures. Only 3.5 per cent died, either from tuberculous meningitis, amyloid disease or other causes. The severe cases may require ten months' treatment, but persistence will be rewarded.—*Die Behandlung der sogenannten chirurgischen Tuberkulose durch den praktischen Ärzt, A. Bier, Münch. med. Wchnschr., February 25, 1921, lxviii, 243.*

Treatment of Surgical Tuberculosis with Turtle Bacilli.—Patients are being given subcutaneous or intramuscular injections of living turtle tubercle bacilli. Fistulae are treated by direct application into the tract. The dose is from 0.25 to 0.3 cc. of a homogeneous suspension of the germs. The concentration of the suspension is not of great moment, as the bacilli are avirulent and nontoxic. The intramuscular injections are made into the gluteal or deltoid muscles. If the hard nodules arising at the site of injection become softened, raying with direct sunlight or roentgen ray (with a 2 mm. aluminum filter) soon restores them to their previous hard condition. With three exceptions, all cases so far treated have been ambulant. No ill effects have been noted, with the occasional exception of a slight temporary rise in temperature. The result, especially in children, is a prompt "fixation of toxin" manifested by a disappearance of night sweats, an increase in appetite, an increase in weight and prompt improvement of general appearance. It is alleged that the cold-blooded tubercle bacillus vaccine is a specific for tuberculosis and scrofulosis. The prognosis is better the earlier treatment is commenced.—*Über die Behandlung der chirurgischen Tuberkulose mit Ktb Vakzine, Brandenstein, Münch. med. Wchnschr, July 2, 1920, lxvii, 786.*

Surgical Treatment of Tuberculosis of the Spine.—The Albee operation consists in transplanting a portion of tibia to replace the spinous processes of diseased vertebrae.

Over 100 cases have been so treated, but this report deals with only 60, operated upon from September, 1913, to August, 1918. All cases of unhealed tuberculosis of the spine were subjected to this treatment; the only contraindications being the contamination of the operative field by fistulae or wounds, the occurrence of paralyses or the generally poor condition of the patient. The ages of the cases varied from one to forty-eight years, but the larger number (44) were ten years or under. A questionnaire was sent out at the end of 1919 to all operated patients. Only fifty-seven cases could be considered, as two had died within a year after the operation, and in one the graft had not taken. All but eight of these were traced. Of the 49 remaining, 42 showed apparent and 26 permanent healing. Such bone implantation is a procedure without serious technical difficulties which offers the patient early and permanent healing. If deformity has not already been established it is prevented; if kyphosis exists its further development is arrested. No interference with movement of the body is experienced.—*Über unsere Erfolge mit der Albeeschen Operation in 60 Fallen von Wirbelsäulentuberkulose, Görres, Münch. med. Wchnschr., July 30, 1920, lxvii, 896.*

Care of Tuberculous Cripples.—Essential points in the care of tuberculous cripples are (1) the child should be brought under treatment as early as possible, (2) treatment should be prolonged for a sufficient length of time to obtain the best cure, (3) after-care must be provided to guard against relapse, a provision most readily effected by arrangement with the School Medical Officer, and (4) suitable educational provision must be provided to stimulate recovery and prevent mental stagnation. As a result of his experience the author made the following suggestions: 1. The introduction of special teaching in the medical schools and facilities for post-graduate study. 2. The inauguration of a diploma in tuberculosis in order that specially trained officers may be available for the work. 3. The centralization of the work for nonpulmonary tuberculosis under one head, namely, the Medical Officer of Health and his Surgical Tuberculosis Officer, as against the multiplication of responsibilities which now exists. 4. The treatment of these cases in special hospital schools and residential open-air schools, as against their reception into the wards of the general hospitals and the convalescent homes. 5. The establishing of after-care clinics and the necessary machinery for following up cases which have undergone treatment, in order that the results obtained from the treatment of this disease may be most effectively checked up.—*The Care of Tuberculous Cripples: A Proposed Scheme, T. H. Martin, Brit. J. Tuberc., July, 1921, xv, 112.*

Extrapleural Thoracotomy.—The following is a report of the only case of extrapleural thoracoplasty done at the Massachusetts General Hospital: A man, aged thirty-four, was referred to the hospital July 28, 1920. He gave a history of eight years' duration. Twelve weeks before entering the hospital he became acutely ill with cough, sputum, night sweats, poor appetite and rapid loss of weight. He presented all the clinical signs of advanced pulmonary tuberculosis on the right side, with no signs of involvement on the left. These findings were confirmed by X-ray examination. The operation was performed August 3, 1920, after the method of Paulsen and Saugman. The patient was comfortably placed on the operating table, with a pillow under his chest. His right arm was extended over his head and the right side of his chest came exactly at the edge of the table. Preoperative medication was as follows: 1.40 P.M., morphine sulphate gr. $\frac{1}{4}$; 2.10 P.M., morphine sulphate gr. $\frac{1}{5}$; 4.10 P.M., morphine sulphate gr. $\frac{1}{5}$. Regional and mass infiltration local anesthesia was used with 1 per cent and 0.5 per cent novocaine-adrenalin. An attempt was made first to block each intercostal nerve by introducing 5 cc. of the 1 per cent solution in the sulcus intercostalis at the neck of each rib. Then mass infiltration of the region of the incision was done, in which 100 cc. of the 1 per cent and 60 cc. of the one-half per cent solutions were used. The incision extended parallel to and about 3 cm. from the spine, then laterally along the tenth rib. The incision was painlessly made and the scapula retracted outward, giving a good exposure of the ribs. While the assistant controlled the bleeding, the operator, under direct vision, placed more 1 per cent novocaine into each intercostal nerve at the rib angles. Subperiosteal resection of sections of the upper 11 ribs, beginning at the eleventh and working upward, was now done. The ribs were sectioned posteriorly as near the transverse processes as possible, but the operator did not think it important to carry the anterior section too near the sternum. The first rib was so difficult to reach through this incision that only a small section of it could be removed. The sections of ribs removed measured from 2 to 11.5 cm. After the rib resection was completed, the parietal pleura was freed forward and backward from the chest wall, care being taken not to open the pleural cavity. All bleeding was stopped and the muscles sutured. The wound was drained with one rubber dam wick at its lower end. A thick gauze dressing was held in position by adhesive and an especially made chest belt applied at once to compress the right lung. The duration of the operation was an hour and thirty-three minutes. The patient talked throughout the operation and declared he felt no pain. On the fifth day the drain was removed and the wound healed by first intention. The patient left the hospital October 13, 1920, and entered the Cambridge City Tuberculosis Sanatorium at Belmont. The number of tubercle bacilli in the sputum was greatly diminished and the amount of sputum was 45 cc. in twenty-four hours, as compared with 210 cc. on entering the hosptial. The patient gained steadily in weight and in February, 1921, felt so well that he insisted on leaving the sanatorium and returning to work. He began to lose weight almost immediately and in March had two attacks of hemoptysis. In April, 1921, he began hygienic treatment at home, under direction of his physician, and is reported to be rapidly improving again. It now seems assured that the marked improvement shown after operation will result in definite improvement if the hygienic treatment be continued for a sufficiently long time.—*Extra Pleural Thoracotomy for Advanced Unilateral Pulmonary Tuberculosis. Report of a Case, W. Whittemore and G. L. Chaffin, Boston M. & S. J., September 1, 1921, clxxxv, 249.*

Cold-Blooded Tubercle Bacilli and Freidmann's Vaccine.—Moeller administered acid-fast bacteria for the immunization and treatment of tuberculosis before Friedmann. His results as well as those of French investigators were negative. The turtle bacillus is not a cold-blooded type but is a harmless saprophyte. The blindworm bacillus is more closely related to the tubercle bacillus than is the turtle bacillus. Truly virulent human tubercle bacilli can produce immunity to tuberculosis when the initial doses are minimal. Serums of tuberculous patients give the same reaction with grass and turtle bacilli but a much stronger reaction with tubercle bacilli. Serums of rabbits treated with grass or turtle bacilli reveal no difference in the reactions to these two types of bacilli. Furthermore, the grass and turtle bacilli were found to belong to the same variety when using Much's experiment of immunization with "Neurin tubercle bacilli" and by agglutination. By Much's affinity test the grass bacillus was found more closely related to the tubercle bacillus than was the turtle bacillus. Turtle bacilli have no antagonistic relation to tubercle bacilli, as determined by their luxuriant growth on mediums exhausted by the growth of turtle bacilli. Friedmann's bacillus is a saprophyte, grows rapidly, does not adapt itself to the hosts' temperature, does not produce disease after subcutaneous injection, does not multiply in the body and shows no tendency to disseminate. Friedmann's contention that the turtle bacillus produces tuberculosis in cold blooded animals is not verified by Moeller's experiments. The antibodies toward tubercle bacilli are an inseparable unit and can only be produced by living genuine tubercle bacilli; tubercle bacillus emulsions, tuberculins and partial antigens give rise to only a fraction of the antibodies. Immunization with grass or turtle bacilli is impossible, since they lack the pathogenic qualities of tubercle bacilli. Complement binding bodies and agglutinins are not tuberculosis-immune substances but may act merely as a measure for their production. Highly virulent human tubercle bacilli, given intravenously to guinea pigs in a number less than 4 to 5 are soon killed, and produce antibodies. In nine months the animals are accustomed to a thousand times a fatal dose. In two cases highly virulent bacilli were given to patients intravenously without harmful effect. In order to show that turtle bacilli have no antigens homologous to the tubercle bacilli, 30 million turtle bacilli were injected into guinea pigs which were subsequently infected with a small dose of human bacilli. The animals died after six weeks from miliary tuberculosis, as did also guinea pigs not previously treated with turtle bacilli.—*Meine Kaltblütertuberkelbazillen und das Friedmann'sche Mittel, A. Moeller, Berl. klin. Wchnschr., January 24, 1921, lviii, 78.*

The Specificity of Friedmann's Vaccine.—Experimental research has demonstrated that it is not possible to immunize an animal against tuberculosis by the use of Friedmann's turtle bacillus, and that a tuberculous animal cannot be cured of its disease by this means. The clinician must have the last word in the settlement of this question. While it has been conclusively demonstrated that this organism is a saprophyte and in no sense a tubercle bacillus, yet it seems plausible that it may have some value in the treatment of tuberculosis. Antigens other than the tubercle bacillus, such as turpentine, sugar and salt have been used for the stimulation of antibodies in tuberculosis. Is it not possible that the turtle bacillus may play a similar rôle? It has been shown that these bacilli can survive and even multiply in the body for weeks and even months at a time; at the same time many of the germs are being killed. A nodule is formed, so that the pathological condition simulates that of a true tubercle with a persistent source for antibody production. Thus it would seem that the Friedmann bacillus establishes a focus for the continued elaboration of nonspecific antibodies. It remains to be proved whether other nonpathogenic acid-fasts have a like faculty, and whether other chronic infections are influenced by the turtle bacillus.—*Ist die Behandlung der Tuberkulose nach Friedmann eine spezifische? Rietschel, Münch. med. Wchnschr., April 15, 1921, lxviii, 450.*

Treatment of Lupus Vulgaris with Friedmann's Vaccine.—Friedmann's vaccine was administered in 2 cases of tuberculous epididymitis and in 16 of lupus vulgaris. Some of these cases were associated with scrofuloderma, and bone and joint tuberculosis. A remarkable improvement in the scrofuloderma, epididymitis, joint, and bone conditions were obtained; but the lupus vulgaris either was distinctly aggravated or was' not influenced. A difference in the reaction occasioned by Koch's tuberculin and Friedmann's vaccine was noted. The former either produced a diffuse inflammation or swelling and reddening, 1 cm. away from the involved skin, while the latter induced the same changes in the peripheral part of the foci.—*Über die Behandlung des Lupus vulgaris mit dem Friedmannschen Mittel, A. Bushke, Berl. klin. Wchnschr., January 3, 1921, lviii, 3.*

Surgical Tuberculosis Treated by the Friedmann Vaccine.—Fifty-two cases were treated by this method during 1914. The age ranged from one and a half to sixty-nine years, 30 of the cases being under ten years old. The lesions were in bones, joints, lymph nodes, skin and genitourinary system. In 14 this method was exclusively employed; in the rest it was combined with surgical procedures. Injections were made into the gluteal muscles, sometimes repeated once a week or more. A year later 7 of these cases were completely healed, 30 showed temporary improvement, 13 were unimproved and 1 died. Five or six years later 47 of these cases were again followed up. Nine had died, 6 of tuberculosis, and of these 3 died within a month after their discharge. Two died from causes other than tuberculosis. Six patients, although improved, failed to show complete healing. Thirty-two showed no trace of tuberculosis after five or six years. The complete history of one patient with a tuberculous peritonsillar abscess, who responded to the treatment with healing, is given. A case of coxitis, which was treated, relapsed after three months, was again treated and showed marked improvement and absolute freedom from pain. A third case with genitourinary tuberculosis is followed in which the improvement was interfered with by a smallpox vaccination.—*Die Behandlung chirurgischer Tuberkulosen mit der Friedmannschen Mittel und ihre Ergebnisse nach 6 Jahren, F. Krumm, Münch. med. Wchnschr., July 23, 1921, lxvii, 870.*

Inhibition of the Tuberculin Reaction by Serums, Transudates and Exudates.—Transudates, exudates and blood serums, mixed with tuberculin, prevent or weaken the reaction occurring after Pirquet test or subcutaneous injection. This effect is not due to antituberculin but to a colloidal inhibition, being a physical and not a biological phenomenon. The fluids from cases of tuberculosis, carcinoma, acute pneumonia and hydrops, and solutions of casein and colloidal iron all had the same effect. Glucose, however, had no such effect. Charcoal had been previously found to act like the colloids.—*Die Behinderung der Tuberkulinreaktion durch Serums, Transudat und Exudat, L. Dünner and A. Horovitz, Berl. klin. Wchnschr., June, 20, 1921, lviii, 665.*

Therapeutic Value of the Ponndorf Tuberculin Treatment in Pulmonary Tuberculosis.—Ponndorf's technique was not strictly adhered to, in that primarily only two or three small cuts barely deep enough to cause bleeding, were made in the skin of the upper arm previously and a small drop of undiluted tuberculin (O. T.) was well rubbed into the abrasions. At the same time, guided by the skin reaction and the general or local inflammatory reaction, the second vaccination administered after three or four weeks was performed on the other arm through from six to ten cuts about 3 cm. long. Subsequent inoculations were made, differing in the individul cases, usually after an interval of four to six weeks, but always in a new portion of the upper arm: more than two drops of tuberculin in one vaccination site of ten cuts was never used. A preliminary Pirquet test was found advantageous in determining the skin reactivity, which was an index of the allergic immunity. If this proved negative in an advanced case with active clinical findings, active immunization was not feasible. Thirty cases of moderate tuberculosis were treated: 5 were Turban I, 18 Turban II and 7 Turban III;

27 with bacilli in the sputum; and four with tuberculous laryngitis. Of these 30 cases, 11 were markedly benefited, 8 definitely benefited, 8 uninfluenced, 2 permanently harmed by the first vaccination and 1 temporarily harmed by the treatment, so that it was discontinued in these latter three cases. Of the 27 open cases, 9 became rid of bacilli in the sputum. The best results were obtained in the milder cases in the first and second stages, but good results were also obtained in third stage cases. Compared to the ordinary injection methods the cutaneous vaccination (*Kutanimpfung*) had the advantage that marked tuberculin reactions with fever and inflammation occurred less frequently and were milder. Individual cases varied as to the duration of treatment necessary but the average duration was about four months. In certain cases the therapeutic effect was enhanced by concident intravenous calcium chloride injections. The Ponndorf method of cutaneous vaccination is recommended in all cases suitable for active immunization with O. T. The relation between the skin reaction and final success of treatment proved enlightening; of the 24 cases with a moderate or marked skin reaction, 19 yielded good results and of 6 with a weak or negative reaction, 3 were uninfluenced by the treatment and 3 became worse.—*Über den therapeutischen Wert der Ponndorfschen Tuberkulinhautimpfung bei Lungentuberkulose, Leichtweiss, Beitr. z. Klin. d. Tuberk., March 1921, xlvii, 37.*

Tuberculin in the Treatment of Pleurisy with Effusion.—It is questionable whether repeated thoracentesis does not effect more harm than good, for it has been shown that pleural effusions contain antibodies; and by withdrawal of the fluid the body is deprived of the defensive mechanism which it has elaborated. The use of tuberculin increases the number of these antibodies, and the dangers of thoracentesis are avoided. A case is cited with details of the treatment. The patient was having fever and had fluid to the level of the middle of the scapula. Oliguria was a marked feature. After six weeks of treatment the man was able to return to work, free from signs and symptoms. At the outset the daily urine output was 700 or 800 cc; a subcutaneous dose of 0.0002 mgm. of old tuberculin was administered and the next day the urine rose to 1100 cc. Tuberculin was repeated every third day in the following doses: 0.0003, 0.0005, 0.001, 0.005, 0.01, 0.03, 0.06, 0.06, 0.08, 0.2, 0.3, 0.5, and 0.4 mgm. After the twelfth injection of 0.3 mgm. the daily void had reached 2370 cc. The temperature at first ranged between 38° and 39.1°C., but after four injections it dropped to 37.5° and after the ninth injection remained below 37°. The fluid in the chest showed a steady decrease; the patient's symptoms disappeared; and on the day following the eleventh injection he became ambulant. In commenting on the use of such treatment, Stuhl cautions against the employment of too large doses at the start; tuberculin has a strong diuretic effect and it is possible that the fluid in the chest may be removed too rapidly if a dose as large as 0.02 mgm. should be used at the outset. He also mentions that tuberculin offers a means of differential diagnosis as between tuberculous pleurisy with effusion and rheumatic pleurisy. By its use time is saved, the patient is getting proper treatment if the former condition is present, and the necessity of uncertain laboratory tests, not always available, is obviated.—*Weiter Beitrag zur Tuberkulinbehandlung der Pleuritis exudativa tuberculosa, C. Stuhl, Münch. med. Wchnschr., April 29, 1921, lxviii, 514.*

The Leucocytes during the Treatment of Tuberculosis with the Deycke-Much Partial Antigens.—A definite leucocytosis in tuberculosis, except in the severe cases, occurs after the administration of minimal doses of partigens, without a coincidence rise in temperature. This behavior of the total leucocytes was found to be of no prognostic value. The partigens produced a definite lymphocytosis, but this also proved of no prognostic or therapeutic significance in man. Eosinophiles responded variably. If the injections were well tolerated and the case ran a favorable clinical course, they would increase after every injection and would remain thus. In clinically doubtful or unfavorable cases there resulted either no increase or, after a transient rise, a distinct diminution in number. If no reaction occurred and the eosinophiles would diminish, the case was unsuitable for partigen therapy. The reaction of the eosinophiles is, therefore, of prognostic value and can be used as a gauge in therapy.—*Über das Verhalten des Blutbildes, speziell der eosinophilen Leukozyten bei der Tuberkulosebehandlung mit Deycke-Muchschen Partialantigenen, F. Luithlen, Beitr. z. klin: f. Tuberk., March, 15, 1921, xlvii, 20.*

Treatment of Tuberculosis with Partial Antigens (Deycke-Much).—The treatment was tried on 156 cases which had previously been under observation for several weeks. One hundred and forty-six were uncomplicated pulmonary cases; 10 showed bone and gland lesions only. The former were classified clinically as cirrhotic, cirrhotic-nodular, nodular, or nodular-pneumonic types. Eight days before commencing treatment, all patients were given intracutaneous tests with the several antigens, M Tb R, A, F and N; these were repeated two or three weeks before the end of the treatment. Twenty-five patients were treated with the partial antigens, A, F, and N only, while the remainder received M Tb R only. In a first small group of ten the initial dose was determined by the reaction to the intracutaneous test; the second group was likewise started in this manner, but later the highest dilution (0.1 cc. = 0.000,001 mgm.) was employed. The average duration of treatment was five or six months. Most of the cases were kept at rest and all were given the usual dietetic and fresh air treatment. The authors conclude that the treatment is only beneficial as an adjunct to the usual dietetic and hygienic measures in incipient cases; and that even in these it is in no way superior to the ordinary tuberculins. They add that no ill effects have been observed. For diagnostic purposes little insight is gained as to the action of the defensive mechanisms of the body.—*Erfahrungen über die Partialantigenen (Deycke-Much), L. Jacob und M. Blechschmidt, Münch med. Wchnschr., April 1, 1920, lxvii, 447.*

Influence of Organ Extracts on Tubercle Bacilli.—Tubercle bacilli, treated from three to five days with ox or guinea pig lymph node extract or press-juice, were less virulent for guinea pigs than tubercle bacilli in saline suspension. Pancreas and kidney tissue had a similar effect, while the action of muscle juice was negative. Suspension in pleural and ascitic fluids appeared to have no effect on virulence. No delay in the tuberculous process of an infected animal was caused by injection of any of the organ extracts which lowered virulence.—*Experimentelle Untersuchungen über die Einwirkung von Organen, Organextracten, Exsudaten und Sekreten auf Tuberkelbacillen im Reagenzglase und entsprechende Heil- und Immunisierungsversuche gegen die Tuberkulose der Haustiere, C. Giese, Zeitschr. f. Immunitätsforsch. u. exper. Therap., June 4, 1921, xxxi, 533.*

Tebelon in the Treatment of Surgical Tuberculosis.—Tebelon is a proprietary preparation consisting of the isobutyl esters of fatty acids from the tubercle bacillus. Stoeltzner, who isolated the substance, believes that it stimulates the production of antibodies against the waxes of the tubercle bacillus. The results on 19 cases are reported, including bone, joint, gland and skin lesions. Complete healing occurred in 10, within one and a half to three months. Not only were fistulae closed, but by X-ray there was evidence of regeneration about areas of osteosclerosis. Five cases were improved, while in 4 the condition remained the same. The usual surgical and orthopedic measures were continued during the tebelon treatment. Cases showing a positive Pirquet reaction before treatment showed none after its completion. One cubic centimetre was injected subcutaneously into the back every third day. No ill effects attended its use. The author is at a loss to explain the lack of fever if antibodies are formed which are capable of dissolving the capsule of the bacillus.—*Tebelon in der Behandlung der chirurgischen Tuberkulose, W. Baensch, Münch. med. Wchnschr., August 27, 1920, lxvii, 1009.*

Tubar, another Tuberculosis Vaccine.—Koch has established the fact that there is an immunity to tuberculosis, and that for the production of such immunity the intact tubercle bacilli cannot be employed. Deycke and Much have further shown that the water soluble fever-producing elements in the tubercle bacillus (proteins), the chief components of Koch's tuberculin, are not sufficient to accomplish this purpose, but on the other hand that on the removal of these fever-producing substances the establishment of immunity is disturbed. These doctrines were scientifically supported by serological data showing that "partial antigens" would stimulate the production of "partial antibodies," and further, that there existed in the skin a "partial susceptibility" to "partial toxins." Because of the necessity of employing three separate antigens and because of some adverse criticism of the new methods, many physicians have hesitated to adopt the Deycke-Much method; nevertheless the antigenic qualities of the fat components must remain undisputed. In Strubell's laboratory a method was devised for the "feeding and fattening" of staphylococci and tubercle bacilli, with great consequent increase in the lipoid content, and then these "fattened" bacilli, by grinding, were freed from their toxic protein content (the fluid thermogenic element of tuberculin, the "L-Component" of Deycke-Much, or the toxin-component of Maragliano). To this product the name of *Tubar* has been given. Tubar has been employed as a vaccine for three and a half years by Strubell and his colleagues with great success. It is used in dilutions of from 1 to 100,000 million to 1 to 10,000 million in doses of 0.25, 0.5, 0.75 and 1.0 cc.

subcutaneously. A course of 32 injections is used in daily or weekly doses. It is often necessary to repeat the course of treatment once or twice with an interval of six or eight weeks intervening. Cases showing much clinical activity are not amenable to treatment. Defervescence of patients with high initial temperature occurred after the fourth dilution was administered. Cough, expectoration and auscultatory phenomena also disappear. No ill effects have been noted, with the exception of a mild hyperemia about the diseased focus when the strongest dilutions were used. Hemoptysis has never occurred. Tubar prepared from bovine bacilli gives a stronger reaction when injected intracutaneously than does that from human bacilli. Tubar offers the advantage that it is a *single* antigen applicable to the ambulatory treatment of tuberculosis patients of types I and II.—*Über die Masttuberkelbazilleneinheitvakzine Tubar, A. Strubell, Müch. med. Wchnschr., February 25, 1921, lxviii, 239.*

Effect of Fats on Acid-Fast Bacteria.—An emulsion of chaulmoogra oil from *Teraktogenus Kurzii* in chaulmoogra oil soap was used with favorable results on three leprosy patients. The emulsion was of high dispersion and well tolerated on intravenous injection. The soap appeared to be the more active constituent, as nearly clear Berkefeld filtrates from such emulsions were almost as effective. The action of the sodium soap of chaulmoogra oil on various acid-fast microörganisms was found to be as follows: Growth of the avian bacillus in glycerol broth was inhibited by a concentration of 1:500,000, the oil being in this respect 25 times as effective as tricresol, 50 times as active as phenol, and one-fourth as effective as potassium gold cyanide. The tubercle bacillus of the human type was inhibited at a concentration of 1:200,000, while 1:100,000 was required for a number of saprophytic acid-fast bacilli. Non-acid-fast bacteria, such as B. subtilis, B. anthracis, B. typhosus, and Staphylococcus aureus proved to be much less susceptible. Oils similar to chaulmoogra oil in composition, but of different origin, from various members of the plant family *Flacourtiaceae*, had a similar specific action on acid-fast organisms. Codliver oil was also highly inhibitory to the same group. When these oils were treated with iodine this effect was to a large extent lost, unsaturation thus being apparently a vital factor in their bactericidal or inhibitory action. Tuberculous patients, given chaulmoogra or codliver oil, reacted with fever, probably because of the destruction of bacilli and liberation of toxin. Therapeutic indications are therefore similar to those for tuberculin. The favorable effect of codliver oil in tuberculosis is chemotherapeutic, not tonic.—*Chemotherapeutische Versuche mit Fetten an Kulturen säurefester bacillen, A. Lindenberg and B. R. Pestana, Zeitschr. f. Immunitätsforsch u. exper. Therap., June 20, 1921, xxxii, 66.*

Sulphur Dioxide and Tuberculosis.—Practically all men exposed to inhalations of sulphur dioxide are immune to tuberculosis. This known fact has led physicians to experiment with the gas in treating tuberculosis and the treatment is still in the experimental stage. Only incipient cases should at first be selected. The gas is neither irritating nor harmful if care is used in its administration. Failure in treatment is due to several causes: (1) unsuitable cases, that is, longstanding chronic cases and those too far advanced; (2) fibroid phthisis; (3) using the gas too strong, or too often, or prolonging the time for inhalations; (4) using impure gas. Only the pure gas, made from powdered sulphur, should be used. This gas is liquefied under pressure and sold in tanks. A pound will last a month. The patient shows marked improvement within a day or two after beginning treatment. In about two weeks' time he hardly coughs at all except for a few minutes on arising in the morning. He then gets rid of the mucus which has accumulated during the night. The temperature and pulse come down and the patient increases in weight. He must be impressed with the fact that care must be exercised in taking the inhalations or he may add to his already irritated lung condition. Usually three inhalations a day of from fifteen to twenty minutes' duration are sufficient: one on getting up in the morning, one before the midday meal, and one late in the evening. After he has shown marked improvement, the noon inhalation may be omitted. The strength of the gas should be about five parts per million of air. Some patients, after an inhalation, get a fit of coughing when they go out in the open air. These patients are advised to stay indoors for fifteen or twenty minutes before venturing out of doors. Patients at all times must refrain from much talking.—*The Treatment of Pulmonary Tuberculosis with Sulphur Dioxide, F. Tweddell, Med. Rec., August 27, 1921, c, 367.*

Ocular Tuberculosis Treated with a Gold Preparation, Krysolgan.—This preparation is no panacea, but when employed in conjunction with other well-recognized measures in treatment of tuberculosis of the eye, it has proved remarkably beneficial. Its action consists in the stimulation of the formation of granulation tissue; although some have maintained that in the tissues it was bactericidal because of its katalytic action. The author treated 168 cases of various types of tuberculous eye lesions by krysolgan and tuberculin combined, and although he gives no statistics he says that it is his firm belief that this form of treatment is second to none. In many he obtained healing, with or without preservation of function. In two cases of sympathetic ophthalmia the process in the second eye was stopped in three and four days respectively by such treatment.—*Weitere Erfahrungen mit Krysolganbehandlung tuberkuloser Augenkrankungen, O. Schnaudigel, Münch. med. Wchnschr., May 13, 1921, lxviii, 575.*

Test of Cure in Pulmonary Tuberculosis.—When can a patient be considered cured? Neither physical examination nor X-ray information can give unquestionable assurance that a tuberculosis is cured. Too much importance must not be attached to positive tuberculin and complement fixation reactions. As a preliminary requirement in establishing a diagnosis of relative cure, we must demand an absence of bacilli in the sputum after it has been homogenized and centrifugated. Inoculation of the sputum into a guinea pig should be negative; also the protein reactions. Total absence of expectoration, though desirable, cannot be required. The weight and blood pressure must be satisfactory, and constant for a long time. There must be no prolonged rise of temperature after muscular exercise. There must be no morbid respiratory signs. Very important among these signs is a long absence of morbid sounds during prolonged inspiraton following a cough, either in the *zone d'alarme* of Chauvet and Sergent, or in the sternocleidomastoid fossa of Ramond, or at the external border of the subclavicular crux, at the anterior border of the trapezius, where the first abnormal signs appear. But, should all these signs be favorable, can the patient return to work? If there is absence of symptoms for a year or more the patient should be given the progressive work test. It extends over three months, beginning with a few hours' work every second day. The number of hours is increased gradually, and during the third month work is continuous. Since 1904, there have been 432 patients, considered cured, submitted to this test. Of these, 322 have maintained their relative cure, some for as long as eighteen years. There have been 110 relapses. The patients have had both active and sedentary occupations in city and country. Occupations requiring great exertion were excluded. The time of year most favorable for beginning the test is the end of summer or the beginning of autumn.—*Une épreuve de guérison de la tuberculose pulmonaire, L. Rénon, Rev. d. l. tuberc., 1920, i, 20.*

A Prognostic Classification of Pulmonary Tuberculous Lesions.—Fränkel has attempted to make a classification based upon pathological alteration which will express at the same time the prognosis of the case in question. The following points are determined: 1. Open or closed type of lesion. 2. Degree of fever. 3. Extent and distribution of the disease. 4. Anatomic form of lesion: (1) cirrhotic, cirrhotic-nodular, nodular-cirrhotic; (2) (acinar) nodular; (3) lobular, exudative and lobular caseous (bronchopneumonic); (4) lobar, caseous (pneumonic), and (5) presence or absence of cavities. Those anatomic types of lesion with favorable prognosis are placed first, under heading 4, while the more unfavorable types are in a lower classification. After a discussion of several previous classifications made by pathologists, he finds them inapplicable to the clinician's needs and suggests the above. An experienced diagnostician with the aid of the X-ray should be able to so classify his cases before death.—*Ein Schema zur prognostischen Einteilung der bronchogenen Lungentuberkulose auf pathologisch-anatomischer Grundlage, A. Fränkel and S. Graff, Münch. med. Wchnschr., April 15, 1921, lxviii, 445.*

The Prognostic Significance of the Cutaneous Reaction to Old Tuberculin and to Partial Antigens in Tuberculosis.—After a review of the literature, the author deduces the following fundamental principles upon which he bases his theory of the skin reaction in a tuberculous individual: 1. The cutaneous tuberculin reaction is strong because many antibodies are present and, therefore, from combination with the antigens, anaphylotoxin is split off. 2. The cutaneous tuberculin reaction is weak or absent, (1) because too few antibodies are present allowing the absorption of much of the antigen, (2) because so much antibody is present that the antigen is quickly reduced to a nontoxic end-product, (3) because of the absence of tuberculosis and a consequent absence of antibodies, and (4) because of nonspecific influences. In attempting to obtain information of value in prognosis, Kammerer used intracutaneous old tuberculin in dilutions of 1:100, 1:1,000, and 1:10,000. Careful note was made of the extent of the infiltration, the extent and intensity of the erythema, and the occurrence of vesicles, pustules, necrosis, nodulation, lymphangitis and lymphadenitis. The clinical material consisted of a large number of cases which were either definitely nontuberculous suspected of being tuberculous, or were proved to have tuberculosis of various degrees of severity. Readings of the skin reactions were made daily, but most frequently on the fourth, fifth and sixth days. After an analysis of all the cases, Kammerer concludes that only the strong reactions are of value in determining a prognosis, for reactions of a moderate grade (neither strong nor weak) occur in fully 50 per cent of all the cases which manifested all the stages of progress. This failure led to a repetition of the tests, using Much's partial antigens, both the M. Tb. R. (the lactic acid residue of tubercle bacilli) and the single antigens, A., the albumin, F., the fatty acid lipoids, and N., the neutral fats. The M. Tb. R. was used in three dilutions, 1:10 million, 1:100 million, and 1:1,000 million. The reactions on cases of all types were weak and confusing. Seventy-eight patients were then given simultaneous intracutaneous injections of A., F., and N., in the following strengths: A. 1:10 million, F. 1:10,000, and N. 1:1,000. Most of the cases were clinical pulmonary tuberculosis in various stages. A few were nontuberculous, but no clear cut evidence of value in prognosis was obtained. The author states that on the whole he thinks that partial antigens are less serviceable than old tuberculin for purposes of prognosis. He then considers briefly the work done by various investigators on the effect of nonspecific influences on the tuberculin skin reaction. Among such substances he mentions potassium iodide, thyroid extract and benzol, and typhoid inoculations which have been used experimentally to influence the condition of allergy in animals. Moreover, he mentions the influence of acute infections, old age and malnutrition. He shows that when the body is vigorously engaged in the desaturation of antigen the cutaneous reaction becomes weakened, not only to the specific antigen used, but to others as well. On the face of such frequent nonspecific influences which affected the reaction, he was led to seek a solution of the problem in the so called "sensitizing reaction" with O. T. This consists in the injection of a given dose of O. T. and repeating the dose in 8 days, perhaps in the opposite arm. The second reaction is very much more severe than the first, as the result of the sensitizing action of the first dose; a condition, analogous to anaphylaxis, results from the second injection. He considers the mechanism to be a mobilization of antibodies from the focus through the circulation to the skin rather than a sudden new formation of antibodies. One hundred and three cases were given primary injections of O. T. in three dilutions (1:100, 1:1,000, 1:10,000), each 0.2 c.c. in the right arm. Controls were made daily for five to six days. On the eighth day the same doses were repeated in the left arm. Sixty-six of the cases showed an increased reaction to the second dose, while 37 were of the same strength or decreased. The striking feature, however, was that 52 of the 66 cases with increased reaction showed a very rapid development, with an equally rapid subsidence of the local signs. This is again proof of the anaphylactic nature of the reaction, he thinks, and may be explained as a rapid and complete destruction of the protein molecule. From an analysis of his results he concludes that in cases having a favorable prognosis the second reaction will be increased, while the unfavorable case will show a second reaction, either the same as the first or less in degree. The healthy individual or one with only slight disease reacts definitely and strongly to the second injection because the sensitizing dose either mobilizes antibodies or new ones are formed. The sensitizing reaction was likewise repeated, using Much's partial antigens in the same manner, but it was difficult to differntiate between mild and severe types of cases. Likewise, O. T. and partial antigens were used in combination, but without any particularly striking results.—*Was bedeuten die kutanen Reaktion mit Alttuberkulin und Partialantigenen. für die Prognose der Tuberkulose? D Kammerer. Münch. med. Wchnschr., March. 1920, lxviii. 375.*

Scientific Methods for Obtaining Tuberculosis Morbidity and Mortality Statistics.—Besides the measures in general use for learning the number of tuberculous persons, there is one which ought to be made compulsory by all governments, namely, a rigorous bacteriological examination of the sputum of all persons. Only in this way can almost every case of tuberculosis be brought to light.—*Les méthodes scientifiques de diagnostic clinique de l'infection bacillaire aux différents ages, en vue des enquêtes a entreprendre dans les divers pays sur la morbidté et la moralité par tuberculose, M. L. Renon (France), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 41.*

All children should be methodically tested by tuberculin. After ten, examination by X-rays should take the first place, and as these examinations should be general there ought to be adequate provision for X-ray and bacteriological laboratories. Free dispensaries should be everywhere, and civil and military medical bodies should be organized for systematic research.—*G. A. Alfaro and J. C. Navarro* (*Argentine Republic*), *Ibid., p. 49.*

The experimental study of tuberculosis should be removed from general research laboratories and carried on in special laboratories that ought to be established in all large cities and in some smaller ones. From these it should be possible for practitioners to obtain aid in making diagnoses, and it should be obligatory to send to them all suspected material, including the sputa of patients with catarrh. There should be compulsory notification of all germ carriers. Laboratory research ought to include new investigations in the classification of the tubercle bacillus. Its pleomorphism, its acid-resistance during its pathogenic period, its resistance toward all therapeutic measures, and other features possessed by it almost exclusively, all point to the need of a revision in our studies of the tubercle bacillus, a revision which may lead to the discovery of a specific therapy. Its pleomorphism seems to be derived from its efforts at adaptation, and its changing forms are associated with distinct physiological properties which complicate the problem of its study. The germ belongs in the region between the bacteria and the spirochetes. It appears to lie nearer to the latter, that is, it is among the higher bacteria. It is markedly distinguished from its kind by an almost keratinous envelope which furnishes a feature for classification. Four forms may be distinguished: large, short, almost completely segmented germs with an hour-glass-shaped envelope and nearly spherical contents; rods of the classical form with almost imperceptible envelopes; very long rods without visible envelopes. These three forms have five different kinds of grouping: right, obtuse and acute angles, parallels and isolated individuals. Form and grouping are considered together as guides in diagnosis. The first form indicates a condition so grave that cases in which it is seen usually run their whole course within a year; they seldom have hemorrhages, but when they do these are severe. The groups are nearly always right angled, very numerous, and greatly adulterated, especially with pyogenic forms. The second form is associated with slow disease—sclerotic forms of pulmonary consumption. The grouping is acute angled, loose as if the members were about to separate, which they do in the less grave cases. There is sometimes contamination; sometimes not. The third form is seen in less serious cases with long quiescent intervals. The grouping is parallel and the fields are free from contaminating germs. These cases have the most hemorrhages, and it is this and not the evolution of the tuberculosis that constitutes the gravity of cases in which it occurs. In the fourth type, very mild, with long intervals of good health and no fever, the germ is found isolated.—*A. E. y Capo* (*Spain*), *Ibid., p. 52.*

The different parts of the complex problem of tuberculosis statistics ought to be considered separately. An international agreement ought to be established by which the morbidity statistics of different countries would be comparable. The difficulties of diagnosis are so great and so much time is required for a careful diagnosis that the formulation of satisfactory statistics must perhaps wait upon the evolution of simpler methods.—*E. Bachmann* (*Switzerland*), *Ibid., p. 114.*

In Norway the mortality from tuberculosis has diminished greatly in the past seventeen years. The decrease is confined almost to the first five years of life. The same thing has been observed in Sweden and Denmark. An important fact brought out is the constant annual mortality which seems not to accord with acute infection during maturity. Norway requires registration of deaths and of new cases. In limited regions there has been an examination of whole populations. Pirquet tests have demonstrated that the denser the population the greater the percentage of positive reactions. In the free schools of Christiania 80 per cent of the children, seven and eight years old, were positive; and in the country the percentage was 30 to 40 per cent. In some isolated regions where no deaths from tuberculosis were known, 40 to 50 per cent of all the inhabitants gave positive Pirquet reactions, and 50 to 60 per cent gave negative reactions. In the most remote districts not a single child under fifteen reacted positively.—*N. Heitmann* (*Norway*), *Ibid., p. 118.*

Diffusion of Tuberculosis Throughout the World.—Recent work has brought to light the following facts concerning the distribution of tuberculosis. In 1908 Cummins found it absent among the natives, with the exception of a few imported cases, in the Sudanese province of Bahr-el-Ghazal.

Ziemann did not find it in the Kamerun Hinterland, among the Douali tribes, but it was quite frequent in Natal, among the Zulus, in the Transvaal and in Madagascar; while it existed with almost the same intensity as in Europe in all the urban populations of North Africa, but was rare among the Arabs and Berbers who lived as nomadic tribes south of the Atlas Mountains. In 1911 Otto Peiper observed that tuberculous infection was very rare among the negroes of East Africa who lived in huts in the native villages and who did field work, but it was common in the communities where these people came in contact with Hindus, Arabs and Europeans: for example, at Kilua, in a single school, 23 per cent of negro children, 100 per cent of Hindu children and 20 per cent of Arab children gave positive Pirquet reactions, while in the same locality adults reacted in the proportion of 17 per cent among the negroes and 25.4 per cent among the Hindu immigrants. In the Kamerun 3.6 per cent of the adults were infected; but tuberculosis has since made rapid progress here, propagated by commerce and the return of transient immigrants. Throughout West and Equatorial Africa there no longer exist peoples who have been entirely spared, except several nomadic tribes who live on the borders of the desert zones of the Sahara and of Nubia. The same is true of Australia and the Oceanic islands. In the cities of Europe infection by the time adolescence is terminated is practically universal. In rural districts, except where the population is comparatively dense, the proportion of the infected is often much less. In a French east coast village, Stephen Burnet, submitting seventy-five children, from 0 to 10 years, to the tuberculin test, found none infected at the age of five, two at six years, four at seven years and nine in the tenth year. On the other hand, Hillenberg, in a part of Germany where pulmonary tuberculosis is very rare, testing eight hundred and ten healthy children, got 20 per cent of positive reactions from six to ten years and 31.5 per cent from eleven to fifteen years. The studies of Metchnikoff, Burnet and Tarassewitch, among the Kalmuks, a pastoral people of the Volga basin, showed that in the central part of the Steppes, a region where few of the inhabitants lived in cities, 69.4 per cent of the adult men and only 30.6 per cent of adult women reacted positively, while at the border of the territory, where commercial relations with the Russian population are very active, the men gave 95.7 per cent and the women 88.5 per cent of positive reactions. Isolated peoples have comparatively slight resistance to the disease. For instance, among the Senegalese who came to France during the war, and the youth of Bosnia and Herzegovina who were drafted into Austrian regiments, the disease frequently took a fulminant course which was analogous to what we observe in Great Britain and France among young children exposed to massive familial infection. On the other hand, the Jews, in the miserable environment of the ghettos of Lemberg and Cracow, are more resistant. Human tuberculosis is therefore a consequence of civilization. The same features are true of animal tuberculosis. The wild cattle of Madagascar or of the Argentine pampas were free from it. Domestication has caused it to appear among them, and it has become more frequent and more serious among the herds submitted to prolonged confinement in stables than among those who pass their existence in the comparative freedom of the pasture. Human tuberculosis is distributed throughout the world exclusively by the sowers of virulent germs. In the greatest number of instances these are consumptives who spread infection through sputa and excreta. But these are not alone to blame; for it has been established that many apparently healthy subjects, the bearers of latent or occult lesions, and detectable only by tuberculin reactions, intermittently eliminate bacilli with their glandular and intestinal excretions and thus scatter infection. Schroeder and Cotton, as long ago as 1906, showed that calves eliminate bacilli in their dejecta, while Calmette and Guérin, and Joest and Emshoff have demonstrated the frequency of the elimination of tubercle bacilli through the bile of both naturally and artifically infected animals. This work has been confirmed by Breton, Mézie and Bruyant (1912), Titze and Jahn, and Lydia Rabinowitsch (1913), while Nobécourt and Bernard showed the frequency of bacillary elimination by the kidney in different forms of childhood tuberculosis. Bacillary excretion through the mammary gland has been definitely established by many authors; while, if we are to believe the results of a number of observers, it would appear that the case is not different among human beings. The graver forms of tuberculosis may result generally from frequently repeated infections which occur from prolonged cohabitation with intermittent sowers of bacilli. It seems, therefore, that when tuberculosis appears in places where no consumptives are discoverable, it has been introduced by healthy bearers of occult tuberculosis who are distributing virulent germs by their excretions or by certain glandular secretions. Explorers, navigators and merchants have been potent spreaders of infection. While it is without doubt that the manifestly phthisical are the principal factors in the dissemination of the disease, we must nevertheless guard humanity against the possibilities of infection from innumerable people who are in appearance perfectly healthy, but who are slightly infected with lesions limited to the lymph nodes, which may remain indefinitely latent and yet be capable of spreading infection. One can hope to protect the children and populations of countries which are yet relatively spared only by some system which will bring about the general and judicious employment of local tuberculin tests and the clinical examination of the lymphatic system, principally by the X-rays. It is evident that we cannot interdict the social and commercial intercourse of healthy though suspected subjects, yet we may hope to render them inoffensive by appropriate surveillance and education. In every country antituberculosis work and sanitary service must take this direction.—*Les modes de diffusion de la tuberculose a travers le monde, A. Calmette, Rev. d. l. tuberc., August, 1921, 3rd Ser., ii, 235.*

Tuberculosis Statistics, New York City, May-July, 1921.—

	MAY, 1921	JUNE, 1921	JULY, 1921
New cases of pulmonary tuberculosis reported in New York City..............	1,058	1,204	1,105
Total cases of pulmonary tuberculosis on record last day of month......	26,509	26,669	26,890
Deaths from pulmonary tuberculosis in New York City....	469	447	393
New York Tuberculosis Association, attendance at educational exhibit......	2,693	2,561	1,975
Association of Tuberculosis Clinics, new patients examined*	2,011	2,018	1,661
Association of Tuberculosis Clinics, total attendance*.......	10,504	10,176	8,618

* Includes all patients, tuberculous and non-tuberculous.

—*Tuberculosis Statistics, Bulletin New York Tuberculosis Association, September–October, 1921, ii, no. 4.*

Tuberculosis Mortality in New York City According to Sex.—Almost twice as many men as women die from tuberculosis in New York City. Since 1910 the number of deaths of women and female children, from all forms of tuberculosis, has been 31,148, whereas the deaths of men and male children in the same period have totalled 67,748. The percentage is 64 for men and 36 for women. The Federal Census figures now at hand show that the population in New York is practically evenly divided between the male and females sexes, there having been found 2,802,638 males and 2,817,410 females at the time of the enumeration on January 1, 1920. The death rate per 100,000 in each sex is shown in the accompanying table:

New York City—Deaths from all forms of tuberculosis in each sex, 1910 to 1921

YEAR	NUMBER OF DEATHS			DEATH RATE PER 100,000	
	Males	Females	Per cent males	Males	Females
1910	6,352	3,722	63.1	266	155
1911	6,548	3,702	63.9	269	152
1912	6,465	3,516	64.8	261	142
1913	6,362	3,669	64.5	252	145
1914	6,716	3,574	65.3	262	139
1915	6,638	3,611	64.8	254	138
1916	6,185	3,463	64.1	233	130
1917	6,607	3,535	65.2	245	131
1918	6,318	3,780	62.6	231	137
1919	5,346	3,152	62.9	192	113
1920	4,211	2,424	66.0	149	85

In 1910 the death rate in New York City from all forms of tuberculosis was 266 per 100,000 among males and 155 among females. In 1920 it had come down to 149 in the male sex and 85 in the female. The first striking difference, of course, is the constantly higher death rate among those of the male sex; and, secondly, the almost equal decline in both groups, namely, 44 per cent reduction in the death rate among males as against 45 per cent among females. This decline has continued so far this year, and we therefore have the encouraging knowledge that in the past eleven years alone the death rate from tuberculosis in this city in both sexes has been cut in half. Among females, this reduction has occurred even though it began from a much lower point than that of the males. In either sex, the diminution has not yet approached the irreducible minimum.—*Tuberculosis in New York City Attacks Men Especially. Bulletin New York Tuberculosis Association, September–October, 1921, ii, no. 4.*

Tuberculosis among Negroes in New York City.—The problem of the care of tuberculosis in New York is rendered somewhat more difficult by the present large colored population of this city. The Federal census figures, just available, reveal that there are now living here 161,852 colored people. In 1910 they numbered only 93,028. In Manhattan, a large number of them are clustered together in the Harlem district and on the West Side above 59th Street. With the high incidence of tuberculosis in this group of the city's population, the largest clinic attendance is now reported at the Harlem Hospital Tuberculosis Clinic. The deaths among the colored in this city number approximately 625 annually, and the details of the annual mortality since 1910 have been as below:

Mortality, from tuberculosis of all forms, in New York City, among the colored and the white population, since 1910

YEAR	DEATHS		DEATH RATE PER 100,000	
	Colored	White	Colored	White
1910	574*	9,500	617	202
1911	633*	9,617	638	201
1912	643*	9,338	609	192
1913	606*	9,425	542	191
1914	645	9,645	546	192
1915	653	9,596	486	189
1916	574	9,074	440	175
1917	580	9,562	424	182
1918	642	9,456	449	177
1919	706	7,792	471	144
1920	597	6,538	384	119

* From United States Mortality Statistics. The figures since 1914 are from the New York Department of Health Reports.

The death rate among the colored, in 1910, was 617 per 100,000 inhabitants, whereas it was only 202 among the white population. In 1920 it had fallen 38 per cent, and was 384 as compared with 119 among the white. The reduction in the death rate from tuberculosis of all forms in the white population, in the same period, was 41 per cent. In both years the death rate among the colored was more than three times as great as that among the whites. The problem of caring for tuberculosis among the former is therefore much greater than it would be for a white population of the same number.—*Tuberculosis among Colored People in New York City, Bulletin New York Tuberculosis Association, September–October 1921, ii, no. 4.*

Tuberculosis in the South Sea Colonies.—Pirquet tests were made on 760 natives of the South Sea Colonies. The inland villagers having very little intercourse with outsiders (of whom 44 were examined) were all negative. With advancing order of civilization, and thus opportunities for tuberculosis contact, were the *Untere Wariadörfer*, of whom 12.6 per cent were positive; *Morobedörfer*, 13 per cent; *Bogadjimdörfer*, 17 per cent; *Namalos*, 27.3 per cent; *Krankenhaus Friedrich Wilhelmshafen*, 28.2 per cent; and *Sulkasiedlungen*, 32.7 per cent. The positives were always higher among the men than women. Among the children there were very few positive cases. Tuberculosis was not a common disease in these colonies in 1912 and 1913, but civilization, favored by unhygienic conditions, brought it into being. Bovine infection was excluded. The clinical form is mainly pulmonary tuberculosis, and its course is especially rapid and fatal as a result of the absence of a relative immunity in the natives.—*Zur Tuberkulose in der Südsee, H. E. Kersten, Beitr. z. klin. d. Tuberk., March 15, 1921., xlvii, 117.*

Tuberculosis among Catholic Nursing Orders.—In 1889 Cornet called attention to the high tuberculosis mortality in the Catholic nursing orders in Germany, which he attributed to the nursing and especially to infections resulting from careless handling of the sputum. The tuberculosis mortality among the Austrian nursing orders is also high. An analysis of the cases among 2230 sisters and 143 candidates revealed that, of 1852 without hereditary predisposition, 777 (41.9 per cent) developed tuberculosis, while of 521 with hereditary predisposition there were 330 (63.3 per cent). Of the candidates, 39.9 per cent were afflicted, while of the sisters there were 46.5 per cent; which would lead to the conclusion that the first infection in the majority of the cases occurred before entrance to the convent. These figures agreed well with the cutaneous test, which was as frequently positive among the candidates as among the sisters. The kindergarten teachers and other teachers have a high morbidity and are poorly paid, besides being selected from the more intelligent class of individuals. The kitchen personnel has a lower morbidity, the better nourishment being a probable instrumental factor. Repeated infection in the convent is of far more importance than that resulting from nursing. Convent life also reduces resistance and lights up old dormant lesions. Morbidity and mortality are greatest in the younger age groups and diminish with age, which does not agree with the finding among the general female population, where the morbidity and mortality begin to diminish definitely with the climacterium. The ratio of mortality is about the same in all age groups, the deaths being about one-third of the afflicted, the remaining two-thirds recovering and spreading the disease. Of all the afflicted, 414 had pulmonary tuberculosis, 305 caries of the ribs, 77 lymph node tuberculosis, and 36 spinal caries. Blood was expectorated by 401, and only 57 revealed bacilli, probably because of the small percentage whose sputum was examined. The Pirquet reaction was positive in 84 per cent of the new candidates, and in 88 per cent of 482 novices and sisters. Specific treatment seemed to have a slight prophylactic value. Certain recommendations for improvement in predisposition prophylaxis are advocated, including cleanliness in the convents, uniform heating, warmer clothing, increased food including 60 grams of fat daily, graduated work for healthy and ill, baths at least once a week and daily sponges, sleep at least eight to nine hours daily, and prophylactic specific treatment before the appearance of manifest tuberculosis. The recommended exposure prophylaxis includes separate beds for sick and well, early discovery of the disease, sick history book for each nurse, disinfection of beds, clothing and all utensils after every illness, and sputum and cough discipline with the use of sputum cups properly cared for and cleaned.—*Die Tuberkulose in katholischen Krankenpflegeorden, A. Kutschera-Aichbergen. Beitr. z. Klin. d. Tuberk., March, 1921, xlvii, 54.*

Contagiousness of Pulmonary Tuberculosis in Infants.—Two cases are reported, one a girl two and a half years old, the other an infant three months old. The possibility of infection of either of these children by any member of the family is excluded. An older child in each of the families soon developed acute miliary tuberculosis or tuberculous meningitis. It seems fairly certain that the two reported cases were responsible for the development of fatal tuberculosis in the other children mentioned. The sputum in the two original cases was negative for tubercle bacilli on several examinations. The sputum was swallowed. This shows the difficulty of accurate work on the contagiousness of tuberculosis in infants, and the necessity for further research on this subject.—*Sul problema della contagiosità della tubercolosi pulmonare dei primi anni di vita, O. Cozzolino, La Pediatria, July 15, 1921, xxix, 634.*

Tuberculous Infection of a Child.—A boy seven years old, previously negative to tuberculosis by the Pirquet and intracutaneous tests (0.01 and 0.1 gm.), became infected within twenty-four hours, while sleeping in a room in a bed 4 metres from an adult girl who was suffering from open pulmonary tuberculosis with hemoptysis. The boy and a younger brother slept in the room; the older boy (who became infected) played quite a part of the time at the bed of the sick girl but did not kiss her. Both boys after returning home were repeatedly examined by Pirquet and intracutaneous tests. The intracutaneous test became positive after forty-six days in the older boy, while the Pirquet test did not become positive until after sixty-seven days. At no time before or up to a year after infection did the boy show clinical tuberculosis.—*Über Tuberkuloseinfektion, W. Unverricht, Berl. klin. Wchnschr, October 25, 1920, lvii, 1019.*

Danger of Tuberculous Infection in Advanced Childhood.—A rapid acute tuberculosis is described in two children, five and six years of age, in which infection, occurred five and twelve and one-half months before death. It is concluded that in relatively rare cases tuberculous infection, which may rapidly lead to death, can occur in advanced childhood.—*Über die Gefährlichkeit der Tuberkuloseinfektion im höheren Kindesalter, K. Peyrer, Beitr. z. klin. d. Tuberk., March 15, 1921, xlvii, 164.*

The Fate of Children of Tuberculous Parents During the War.—Children of pulmonary tuberculosis parents (patients at the University Clinic of Bonn) were found victims of the same disease in a proportion of 54.2 per cent. In the case of maternal tuberculosis more children were found to be tuberculous than in the case of paternal tuberculosis. In families with a larger number of children the percentage of incidence and mortality is higher than in families with but few children. The highest incidence and mortality occurs in children, one to five years of age, and immediately before and after puberty.—*Über des Schicksal der Kinder tuberkulöser Eltern während der Kriegszeit, J. W. Langendörfer, Ztschr. f. Tuberk., June, 20 1920, xxxii, 150.*

Housing Conditions vs. Food as Factors in the Increased Incidence of Pulmonary Tuberculosis.—In order to ascertain whether the marked increase in incidence of pulmonary tuberculosis in Rostock (a city of 70,000 inhabitants) was due to poor housing or to inadequate food conditions following in the wake of the war, 356 clinic cases of active pulmonary tuberculosis were studied. Their living quarters were classified according to the following standards: number of rooms, lighting, air, cleanliness and number of occupants; whether they contained a kitchen and at least one heatable room; and whether the patient alone occupied the bed. The living quarters of these patients were classed as "good" according to the above mentioned standards in 66.6 per cent; as "moderately good" in 16 per cent; as "poor" in 16.3 per cent; and as very poor in 1.1 per cent. The author does not consider these figures as being sufficiently bad to lay the blame for the increased rate incidence of phthisis upon housing conditions, but by a process of exclusion thinks it due rather to the well known decrease in quantity and quality of food, especially animal proteins, carbohydrates and fats.—*Tuberkulose und Wohnungsverhältnisse, W. Tobias, Ztschr. f. Tuberk., April, 20, 1920, xxxii, 1.*

Influenza and Pulmonary Tuberculosis.—Influenza was studied in 66 cases of pulmonary tuberculosis. All except 3 of these were in classes I and II Turban. In 81.7 per cent the existing pulmonary tuberculosis was not unfavorably influenced; rather, 20 per cent of these showed definite improvement. Healing was in no way retarded by the influenza. In 18.3 per cent the latter exerted an unfavorable influence, causing either an increase of the tuberculous process or detrimentally affecting the general condition (to this group belonged the 3 Turban III cases). In 6 of the 66 (9.1 per cent) cases, the pulmonary tuberculosis was apparently of primary occurrence, but in these there was either a family predisposition, an earlier scrofulosis, or a reduced individual resistance ascertainable. The course of influenza in the author's cases of tuberculosis was mild.—*Grippe und Lungentuberkulose, G. Deusch, Beitr. z. klin. d. Tuberk., November 25, 1920, xlv, 1.*

Influenza and Pulmonary Tuberculosis.—Caseous pneumonia may arise from an old tuberculous focus immediately after influenza, as a result of the entrance of tubercle bacilli into the bronchi. An old inactive focus may become active after influenza and induce progressive disease. In many cases without involvement of the lungs, latent hilum tuberculosis may set up active tuberculosis of the bronchial nodes with caseous pneumonic processes frequently of central location. There is always an interval of health of varying duration between the incidence of influenza and the latter variety of tuberculosis. Knowledge of the consequences of influenza will prevent the progress of a hilum tuberculosis of the lungs by proper treatment of apparently healthy persons in the anergic interval.—*Grippe und Lungentuberkulose, O. Kiefer, Berl. klin. Wchnschr., October 4, 1920., lvii, 951.*

Tuberculous Toxins as Causes of Disease.—Tuberculotoxin involvement of the eye and cerebral nerves in 6 cases were cured by tuberculin treatment. One of these cases was treated previously with mercury, aspirin and potassium iodide without effect, and was markedly improved by nine tuberculin injections. In the other 5 cases, turbidity of the vitreous humor and cerebral nerve paralysis disappeared promptly with tuberculin treatment.—*Die Tuberkulotoxine als Krankheitsursache, G. Hirsch, Berl. klin. Wchnschr., May 23, 1921, lviii, 549.*

The Nose as a Defense against Tuberculosis.—Besides its functions of smell and respiration, the normal nose acts as an important defense against tuberculous infection and against the inroads of established tuberculous disease. In normal nasal respiration, the commencement of inspiration draws the air from the nasopharynx, which causes the air to flow out of the sinuses. This flow continues till the end of inspiration, leaving a partial vacuum in the sinuses. When expiration begins, the last of the inspired air containing oxygen, and occupying the space above the soft palate, is drawn by negative pressure into the sinuses, and it is there held until the next inspiration. Examination of the skulls of lower animals with their infinitely complex turbinate and ethmoidal structures shows that it is next to impossible for the inspired air to pass through this region without coming intimately into contact with their structures. The study of the circulation of the air in the sinuses has shown us there, too, the intimate contact which must take place between the inspired air and the lining cells. Since these lining cells are not only ciliated but constantly moist, the inspired microörganisms must with absolute certainity be deposited on them and digested or otherwise destroyed. On theoretical grounds, therefore, it is impossible for a nose breather to be infected with tuberculosis, since no microörganisms can pass this ingenious filter, if it is in proper working order. Further experiment shows that the capacities of the nasal epithelial cells are not limited to their bactericidal action. If, in a case of tuberculosis, insufflations of suitable dosage of bacillary emulsion of tubercle bacilli are made into the ethmoidal region, certain and constant improvement takes place. This definitely shows that these epithelial cells which line the mucosa in the upper regions of the nose are capable of forming antibodies. Hence immunity in tuberculosis resolves itself down to the establishment of a proper inspiratory current through the upper regions of the nose. Immunity in tuberculosis depends on the proper anatomical relationship of the middle turbinate bone to the septum nasi, and the physiological capacities of the epithelial cells in the upper regions of the nose.—*Immunity in Tuberculosis, O. Paget, Med. Rec., October 8, 1921, c, 627.*

The Origin of the Multinucleated Giant Cell.—The multinuclear giant cell, called the "giant cell of irritation" by Laulanie, while most often encountered in the tubercle, is by no means peculiar to it, being found in syphilis, leprosy, actinomycosis, and many other chronic infectious processes, as well as in the tissue response to the presence of a sterile foreign body. It is a fixed phagocyte. The authors studied its formation in birds and mammals. It is most readily followed in the experimental tuberculosis of fowls. It was noted that in the young tubercle produced by injection of the avian type tubercle bacillus, a portion of the epithelioid cells constituting the lesion were fused into a large syncytium, usually in the centre of the tubercle. In somewhat older tubercles a concentration of nuclei in various portions of the syncytium was seen. This was followed by fissuring of the mass in lines radiating from the centre. In the final stage, contraction occurred in the masses thus separated, with the production of typical multinucleated giant cells, continuous on the one hand with the protoplasmic processes of surrounding epithelioid cells and on the other with the debris of the now caseous centre of the tubercle. The conditions in mammalian tuberculosis are similar, although the process may be complicated by the greater resistance of the host, expressed by the formation of granulation tissue, which with lymph fills in the interstices left on the formation of giant cells by contraction. The movement of nuclei to the periphery of the giant cell is probably a chemotactic adaptation to the conditions of chronic infection, as the reduction in total surface of the many epithelioid cells taking part in its formation is a protection against the destructive influence of bacterial poisons, while, on the other hand, the size is not too large for nutrition by diffusion.—*La cellule géante. Syncytium ou dérivé de syncytium. Contribution a l'étude des granulomes, Liénaux and Hamoir, Ann. de l'Inst. Pasteur, November, 1920, xxxiv, 775.*

Bacteria on Coins.—The object of this investigation was to determine the numbers and types of microörganisms on the coins and currency being used in general circulation. The smaller values were used, since it was believed that these were passing more quickly from one person to another. *Summary and conclusion:* There seems to be little basis for the belief that coins bear any close relation to the spread of disease. The indicators of pollution used in sanitary investigations were entirely absent on the coins used in this investigation. Thirty-seven of the strains of microorganisms isolated from the coins were sporeformers, and probably spores are necessary before the organism may perpetuate itself for any considerable length of time on coins. This may explain why none of the commonly accepted indicators of pollution were found. They are not spore-forming organisms, and consequently are destroyed by the action of the metals. Since the flora of coins seems to be made up almost entirely of microorganisms which form spores it is reasonable to assume that coins might function in spreading diseases, the etiological agents of which are spore formers. It was shown in this paper that Bacillus anthracis was able to live for eighty days on pennies and seventy-one days on nickels when the experiment ended. The greatest factor tending to control the types and numbers of microorganisms on coins seems to be the metal of which the coins are made. Numerous instances are mentioned in the literature where it is shown that the metallic ions have a distinctly bactericidal effect. The same statement applies to certain of the salts of these metals. It is undoubtedly true that coins which are passing from person to person in general circulation come in contact with acids and alkalies which were the formation of soluble salts on their surfaces. These tend to keep down the bacterial flora and to probably exert a selective action, destroying the non-sporeforming organisms. Mold spores were isolated in a few cases. These probably are just as resistant as the bacterial spores, although they play a lesser rôle in the transmission of infection.—*Bacteria on Subsidiary Coins and Currency, Charlotte B. Ward and F. W. Tanner, Am. J. M. Sci., October, 1921, clxii, 585.*

Relative Value of Laboratory and Clinical Methods in Tuberculosis.—The two outstanding needs in medicine to-day are the correlation and unification of the recent scientific discoveries which have been made, and more accurate clinical observation. The opinion seems to be prevalent that laboratory and mechanical means of arriving at truth are accurate, while clinical observation is inaccurate. Yet the laboratory and mechanical measures have back of them the errors incident to the reaction and the apparatus plus the errors of the observer, while clinical observation has the errors of the observer only. There has been too much tendency to reduce things to so called normal standards. Modern medicine with its study along special lines has emphasized disease processes and methods of examination and minimized the patient. The examination of sputum is surrounded by more errors than are usually recognized. The absence of tubercle bacilli does not mean absence of tuberculosis. The disease may be present, even in a widely scattered area, and may be causing marked clinical symptoms without rupture of the tubercles or appearance of bacilli in the sputum. Moreover, the usual methods of diagnosis are subject to greater error than is generally believed. Ordinary methods of treatment and staining of sputum will detect bacilli if present in numbers of 2000 to a cubic millimetre. The most refined method, that of homogenization, will enable one to find them, if present in numbers of 200 to a cubic millimetre. Furthermore, patients with early tuberculosis may expectorate ten times a day, but expectorate bacilli only once. Sputum should be examined for albumin and lymphocytes. The complement fixation test has many sources of error; interpreted in conjunction with other data it is of value. The roentgen ray should be operated and interpreted by experts, and even in the hands of many of these, the result is frequently doubtful. Much help may be obtained from the tuberculin tests. A prompt marked reaction coincides closely with clinical activity. Intracutaneous test with 0.1 to 0.2 cc. of a 1:5000 dilution of Koch's O. T. is to be preferred. None of these methods gives an idea of the patient's resistance to the infection. One may classify the symptoms of tuberculosis into those due to toxemia, those to reflex causes and those to the tuberculous process *per se*. In advanced tuberculosis, symptoms and syndromes resulting from the disease are enumerated. In the first of these groups, general nerve and endocrine disturbances are included; in the second, symptoms due to reflex action; while the third group is most important from the diagnostic point of view. The changes found on physical examination are partly anatomic and partly physiological. The percussion note is modified by all structures adjacent to the lungs. In the apices, from the second rib upward, percussion through the tense muscles is probably more influenced by the latter than by the few tubercles in the lung in early tuberculosis. The same is true of auscultation, though to a lesser degree. Palpation is as accurate as percussion at its best. Different density in the lungs, mediastinum and pleura may be felt by light palpation. The motor and trophic changes in the muscles, skin and subcutaneous tissue, reflexly produced by pulmonary inflammation are visible to the eye and recognizable on palpation. The pulmonary motor reflex expresses itself in the muscles receiving their innervation from the cervical segments of the cord. The pulmonary trophic reflex is shown in the skin, subcutaneous tissue and muscles supplied by the cervical segments of the cord, particularly the third fourth and fifth segments. The motor reflex produces increased tonus-spasm of the muscles and limits the respiratory movements. The pulmonary trophic reflex is indicated in degeneration of these muscles, and of the skin and subcutaneous tissue above the second rib anteriorly and the spine of the scapula posteriorly. These degenerations are evident at a glance and more so on palpation; they indicate chronic inflammation of the lung. Tuberculosis produces the greatest amount of reflex degeneration, although chronically infected bronchi, unresolved pneumonia, pulmonary abscess and other chronic infections may produce some change.—*The Relative Value of Laboratory and Clinical Methods of Study in the Diagnosis of Tuberculosis, F. M. Pottenger, Am. J. Med. Sci., September, 1921, clxii, 352.*

Clinical Diagnosis of Adult Tuberculosis in Czecho-Slovakia.—The character of the infection in the tuberculous must be judged by the sum of all the reactions which he exhibits. We must consider the amount of the tuberculin dose, the local reaction, the form of the temperature curve, the general symptoms, and the focal reaction where this is accessible to observation.—*Méthodes scientifiques de diagnostic clinique de la contagion bacillaire chez l'adulte dans les stations de la République Tchéco-Slovaque, K. Franz (Czecho-Slovakia), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, 1921, p. 119.*

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The Abstract Editor is Dr. George Mannheimer, 41 West 51st Street, New York City. Prompt transmission to him of reprints or abstracts of papers on tuberculosis, sanatorium or board of health reports, etc., will promote their early publication in this section.

Abstracts should be sent typewritten on one side of the page only. They should be as concise and compact as the subject matter of the article warrants. They should be headed with a short title, and followed by the full title of the paper, author's name, journal, date, volume and page.

Classification of Râles.—Examination of most of the textbooks in use in the leading American universities reveals an astounding divergence in the nomenclature of râles. Guthrie advocates simplification. He divides them into (1) crepitant or vesicular, (2) mucous or tube, and (3) cavernous râles. Subcrepitant, sonorous and sibilant types can be classified as subdivisions of the mucous râles.—*Classification of Râles: A Plea for Simplification, J. B. Guthrie, Am. J. Med. Sci., September, 1921, clxii, 372.*

Diagnosis of Tuberculosis in Childhood.—Tuberculosis is not a universal disease in childhood in this country, at least. The universal findings in Europe do not hold in America. The diagnosis of tuberculous infection rests largely upon the skin reaction which is of value at any age. The value of the reaction is commonly lost by careless methods. The activity of tuberculosis must be judged by the temperature curve and by other signs of toxemia, such as malnutrition, anemia, etc. The site of the lesion is often difficult to find. The bronchial nodes are most commonly infected, but give few signs. The best sign of tuberculous bronchial lymph nodes (or of any other inflammatory condition in this region, such as that due to whooping cough or influenza) is D'Espine's sign. From an analysis of 550 cases with reference to this sign, the author concludes that its presence below the third, and especially below the fourth dorsal vertebra, is very suggestive of tuberculosis.—*The Diagnosis of Tuberculosis in Childhood, C. H. Smith, abstracted in Arch. of Ped., July, 1921, xxxviii, 441 (Paper read before the American Pediatric Society at the meeting of June 2–4, 1921).*

Provoked Inequality of the Pupil in the Diagnosis of Early Tuberculosis.—Professor Sergent, who has long made a study of the precocious diagnosis of pulmonary tuberculosis, last April announced the discovery of a possible new sign (*Journal de médecine et de chirurgie pratiques*, June 10, cviii, 11). He terms this "provoked mydriasis." Before that period he had traced a connection between pupillary inequality and the presence of a dry apex pleurisy in which the sympathetic nerve was the transmitting agency. Apparently filaments of these nerves are involved in certain enlargements of regional lymph nodes. In certain cases subsequent miosis was explained by destruction of the said fibres. As a spontaneous phenomenon not much could be expected of it in diagnosis and therefore Sergent tested suspicious cases with mydriatics in both eyes. The latent period is counted as 10 minutes and dilatation reaches its maximum in 25. Upon the theory that the aforesaid lesions will sensibilize the sympathetic on the diseased side the author expected a precocious reaction. Ten normal subjects tested were found to present bilateral symmetry in mydriasis. Of 18 subjects known to have unilateral apical trouble 11 showed inequality. In another series of 22 suspicious cases 15 gave a positive result. In addition to the frankly negative results there were a number more or less anomalous and it would seem that the stage of the lesion and resulting cicatricial changes play a rôle.—*Editorial Note, Med. Rec., October 1, 1921, c, 597.*

Percutaneous Reaction with Highly Concentrated Tuberculin.—Three groups of patients were studied: (1) 52 clinically active tuberculous cases, (2) 9 children living with open cases, and (3) 13 nontuberculous children who entered the clinic for other conditions. Tuberculin concentrated to constant weight, and ordinary O. T. were used. For the Moro test the midsternal region was used. The Pirquet and puncture reactions were done on the lower arm. Of 69 tuberculin positive cases, 58 (84 per cent) gave a primary positive Moro reaction with concentrated tuberculin, while only 36 (51.1 per cent) reacted to ordinary tuberculin. A comparison of both tuberculins in 36 positive Moro cases revealed a more marked reaction with the concentrate in 29 of these. In comparing the concentrate Moro with the Pirquet test with ordinary tuberculin in 55 tuberculin positive cases, 45 were positive to the former and only 42 to the latter. A comparison of the Pirquet test with ordinary tuberculin and the concentrate showed the latter to be only slightly superior (1.8 per cent). The puncture reaction proved inferior (39 of 45 cases positive) to the Moro test with concentrate. The Moro test with concentrate has the advantage of being performed painlessly which makes its use especially desirable in children.—*Über die perkutane Reaktion mit äusserst eingeengtem Tuberkulin, F. Stradner, Beitr. z. Klin. d. Tuberk., November 25, 1920, xlv, 31.*

Lymph Node Reactions to Tuberculin.—After tuberculin injections in the forearm examinations were made of the cubital, axillary, supraclavicular and infraclavicular lymph nodes, besides noting the other reactions usually obtained to tuberculin of 34 nontuberculous cases, injected with 1 mgm. O.T. Only 6 revealed an increase in size of the regional nodes. These included cases of emphysema, enteritis, furunculosis, tenia, rheumatism and scabies. A node reaction was obtained in 10 of 15 closed cases of apical tuberculosis. Of 14 cases given therapeutic inoculations of O.T., 13 gave the node reaction; of 20 cases given albumose-free tuberculin, 6 were negative; of 27 cases given old albumose-free tuberculin only 5 were negative, and of 10 cases given bacillus emulsion all gave strong positive reactions. Clinically negative tuberculous cases gave the lymph node reaction in 18 per cent of those tested, and tuberculous suspects 66 per cent. The node reaction seems to be correlated to the skin reaction, being, however, less sensitive. This reaction seems to have the advantage, however, of determining the presence of an active tuberculosis, while the other reactions merely indicate a previous infection.—*Drüsenreaktion bei Tuberulinimpfung, K. Glaessner, Beitr. z. klin. d. Tuberk., November 25, 1920, xlv, 8.*

Diagnostic Value of Pirquet Test.—The 5044 tested cases were Petruschky's patients in Danzig and West Prussia. The test was made to determine whether tuberculosis was or could be instrumental in producing the manifestations observed in those in whom diagnosis was doubtful. Petruschky's modification of the Pirquet test was used: the left upper arm is cleaned with ether or alcohol and two scratch crosses made not deep enough to draw blood, tuberculin being applied to the upper cross and the lower being used as the control. To the first test 864 reacted negatively, and 444 of these were tested a second time, when 27 per cent reacted positively. With increasing age (in which the tuberculosis incidence is also known to be higher) a greater percentage of positives was found on second test (up to 5 years, 11 per cent; 6 to 14 years, 16 per cent; 14 to 20 years, 29 per cent; 20 to 30 years, 48 per cent; 30 to 40 years, 46 per cent; and over 40 years, 54 per cent). This result is attributed to the more active processes which occur in children and youths, and the encapsulated and calcified nodules, containing relatively fewer bacilli and less capable of releasing specific substances, of those more advanced in age. To the first test 113 reacted questionably, while 82 per cent of these became definitely positive to the second test; the percentage of positives again being greater with increasing age (43 per cent up to 6 years, and 100 per cent over 40 years). A summary of all the cases (5044) revealed 87.6 per cent of positive reactions (up to 6 years, 57 per cent; 6 to 14 years, 78 per cent; 14 to 20 years, 88.6 per cent; 20 to 30 years, 94.8 per cent; 30 to 40 years, 96.8 per cent, and over 40 years, 96.3 per cent). In 965 cases there was no clinical tuberculosis, and of these 72.2 per cent reacted positively (up to 6 years, 52.5 per cent; 6 to 14 years, 60.9 per cent; 14 to 20 years, 68 per cent; 20 to 30 years, 82 per cent; 30 to 40 years, 88.6 per cent; and over 40 years, 84.6 per cent). Of 105 cases of open tuberculosis only 2 were negative, one of these reacting positively on the second test while the other was not tested a second time. Of 1965 closed cases 98.5 per cent were positive. Of 1921 glandular cases and suspects up to 6 years, 56.3 per cent were positive; 6 to 14 years, 80.3 per cent; 14 to 20 years, 86.1 per cent; 20 to 30 years, 92.2 per cent; 30 to 40 years, 93.0 per cent; and over 40 years, 95.5 per cent. Petruschky's spinalgia (*Spinalgie*) was the only symptom of tuberculosis in 4.7 per cent of the cases between 6 and 14; in 19 per cent at 14 to 20 years; 15 per cent at 20 to 30 years, 11 per cent at 30 to 40 years, and 7 per cent in those over 40 years. Comparing the findings in patients without clinical tuberculosis, with spinalgia and with pulmonary tuberculosis it is concluded that spinalgia is an indication of tuberculosis, although not an entirely dependable one. A like comparison of the glandular cases leads to the conclusion that lymph node enlargements in young children are occasioned rather by nontuberculous conditions, while in older children and youths they are mostly, though not always, due to tuberculosis. Every positive tuberculin reaction indicates the presence of tuberculous nodules with living tubercle bacilli.—*Über die diagnostische Bedeutung der von Pirquetschen Kutanprobe an der Hand einer grösseren Statistik, R. Peters, Beitr. z. Klin. d. Tuberk., March 15, 1921, xlvii, 130.*

Blood Lipases in Tuberculosis.—In order to determine whether the fat-splitting ferments of the blood, obtained from various forms of tuberculosis, showed quantitative variations, the tributyrin method of Rona and Michaelis was used. Fibrous forms of tuberculosis gave high, and caseous and exudative types low lipase values. Examinations at intervals, on the same persons, revealed an increased lipase titre when there was an increase in weight and a diminution in the fever, and vice versa. The lipase titre seems to follow the clinical course of the disease, and decreases when there is an accumulation of tuberculous pus in the body (spondylitis, peritonitis and caries). Tuberculin injections influence the titre only in so far as they have a clinical effect. Deep roentgen ray treatment seems to have a profound effect on the lipase titre of the blood. Shortly before death the titre drops to a low value. The lipolytic power of postmortem blood is probably not identical with that occasioned by lipase. Cases of pseudochylous serums revealed no diminished lipase, while disturbances of the endocrine glands produced significant changes. No relation was found between the lipase titre and the lymphocyte count. In tuberculous guinea pigs the titre progressively diminished.—*Die sogenannten Blutlipasen bei Tuberkulose, II Mitteilung, A. Frisch and V. Kollert, Beitr. z. Klin. d. Tuberk., March 15, 1921, xlvii, 146.*

Diagnostic Value of the Wildbolz Auto-Urine Reaction.—Theoretical considerations and a concise review of the literature are followed by a report of the results on 220 cases in which this method was employed, together with control intracutaneous tuberculin tests. The technique consists in evaporating *in vacuo*, at a temperature of 60 to 70°C., 150 cc. of a morning urine specimen. This concentrated urine is placed in the icebox over night and on the following morning it is filtered through sterile paper. Injections are made into the skin of the outer surface of the upper arm, in sufficient amount to produce a bleb 5 mm. in diameter. A positive reaction consists of erythema and infiltration of the skin persisting for at least forty-eight hours. If necrosis of the skin occurs it may be due to trauma or it may be caused by excessive salt concentration (phosphates) in the urine. In this case it is possible to obviate the difficulty by treating the concentrated urine with 20 volumes of 90 per cent alcohol in which the antigens are soluble. The salts are removed by filtration and the filtrate is again concentrated *in vacuo* to the original urine volume. A positive tuberculin test merely indicates tuberculous infection; a positive auto-urine reaction indicates activity of this infection. If the tuberculous patient be in a state of anergy he will not react to an intracutaneous inoculation of his own urine, but if his urine be inoculated into another tuberculous individual who is in an allergic condition a reaction is readily obtained. The test is of great value in differential diagnosis, and 20 surgical cases, all with positive tuberculin reactions, some with positive Wildbolz reactions, are cited. Subsequent operation in every case established the absolute reliability of the auto-urine reaction. In 220 cases, chiefly of tuberculosis in different locations, on which the unmodified Wildbolz procedure of auto-urine inoculation was tried, the claims of the originator of the test was substantiated. For confirmation of the diagnosis, one should always employ an intracutaneous tuberculin test on the same arm. In the case of an anergic patient his urine must be injected into an allergic individual. In case the urine, because of its high salt concentration provokes necrosis at the site of inoculation, the salt may be removed by alcohol without injuring the antigen in the urine. Strongly positive reactions are often found early in the disease; chronic cases and those with extensive destructive processes often present weak skin reactions. The antigen content of the urine does not correspond with the extent and activity of the process. The reaction, as an aid in prognosis, is significant only in so far as the tuberculous process may be active or healed.—*Die diagnostische Verwertbarkeit der Wildbolzschen Eigenharnreaktion, E. Bosch, Münch. med. Wchnschr., June 17, 1921, lxviii, 733.*

The Alizarin Test in Infantile Tuberculosis.—Forty cases were tested by Roncal's method, using a 1 per cent alcoholic solution of alizarin (oxy-anthraquinone). A strongly positive test was characterized by the production of a dusky red color with the formation of a purple precipitate. The color is typical and lasts for some days. Nontuberculous sputum is colored purple red and does not give a precipitate. In twenty normal children the reaction was negative; in forty children suffering from various diseases, the reaction was positive in four with pulmonary tuberculosis, six with peritonitis, two with meningitis, one with adenopathy, one with scrofula, one with erythema nodosum, one with pleural effusion (all of tuberculous origin). The test was applied to the spinal fluid in the two cases of tuberculous meningitis, and was positive. The test as applied to spinal fluid will be made the subject of further research.—*La prova dell' alizarina per la diagnosi della tubercolosi nella infanzia, G. Genoese, La Pediatria, March 1, 1921, xxix, 227.*

Agglutination Reaction in Tuberculous Infection of Children.—Of 235 tuberculous children, 95 per cent gave a positive agglutination reaction with the avian variety of tubercle bacilli. In 5 the titre was 1:200. In the majority, agglutination occurred at 1:25 to 1:200. The reaction was negative in the earliest cases and in cases which had advanced to the state of tuberculous cachexia. There is no definite relation between the amount of tuberculin injected, the agglutination content of the blood, and the condition of the patient. The titre sometimes grew higher as the child improved, and lower as the process became more advanced. The special localization of the tuberculous process apparently had no effect on the reaction.—*Sulla siero-agglutinazione nell' infezione tubercolare dei bambini, R. Kharina-Marinucci, La Pediatria, June 15, 1921, xxix, 529.*

Serum Agglutination of Tubercle Bacillus.—In the adult with a developing tuberculosis a negative agglutinin reaction is a very ominous sign. If there were previous evidences of tuberculosis, but no present symptoms exist, a negative agglutinin reaction indicates complete recovery. A much feebler positive reaction has value in the child than in the adult. In old persons a positive reaction is very frequent because of the great number of present, recent or latent tuberculoses. Consequently, in these a positive reaction indicates lesions recently cured or still active, but a negative reaction indicates the absence of previous tuberculosis or one completely cured. Therefore, in these cases the reaction is useful for making a diagnosis of tuberculosis in evolution, or a latent or a past lesion, which would otherwise be very difficult to detect. One of the important uses of the agglutinin reaction is to determine the moment when an active tuberculous lesion is completely cured, and it is among the best means by which this can be done. The agglutination work in process before the war should be resumed, and, particularly, observations should be made on the same subjects of agglutination, fixation, and cutaneous reactions.—*La séroagglutination du bacilli de Koch, Paul Courmont (Lyons), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 123.*

Diagnostic Methods of Bacillary Infection.—Percussion, auscultation, roentgenology, bacteriology and immunization experiments show different aspects of the state of the lungs, and all should be employed. Auscultation is more valuable than percussion or X-ray examination, but the latter reveal conditions which auscultation does not discover. Immunization experiments and the observation of evening temperatures are equally adapted to confirm a diagnosis of active tuberculosis. In the stations of the Czecho-Slovak Republic an examination is not considered complete unless the subject has been examined by all these methods.—*Méthodes de diagnostic de la contagion bacillaire, L. Syllaba (Czecho-Slovakia), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, 1921, p. 120.*

Properties of Tubercle Bacilli Attenuated by Bile.—Previous work had shown that bovine tubercle bacilli, after prolonged serial cultivation on potato treated with a medium of five parts of bile to one hundred parts of glycerin, gradually lost their tuberculogenic power and underwent a transformation which allowed their use for the immunization of calves against virulent natural or artificial infection by tuberculosis. Furthermore, this increased resistance is maintained as long as the treated animals preserve the living attenuated bacilli in their lymphatic system, but ceases when the bacilli have been eliminated through the natural paths of excretion. The present contribution had as its object the observation of the effects of this bile-treated bacillus upon other animals than cattle which were susceptible to tuberculosis. The work was done with cultures taken from the two hundredth to the two hundred and thirty-fifth passage on the bile medium, cultures which were transplanted every two weeks and incubated at 38°C. These bile-treated bacilli have been so modified, that, if replanted upon ordinary potato-glycerin-broth, they assume the normal appearance of tubercle bacilli, but never regain virulence and remain incapable of producing tubercles. A single subcutaneous inoculation, of 0.5 to 1 mgm., produces neither abscess nor lymph node reaction in guinea pigs: there is only a slight local tumefaction which disappears within two or three weeks without leaving a trace. After similar inoculations of from 5 to 10 mgm. there ensues a very rapid edema, followed by a small abscess, which ulcerates on the tenth to the twelfth day, forming a true chancre which suppurates for from two to four weeks and then heals. Meanwhile, the corresponding lymph node undergoes a slight and transitory enlargement. The infection never becomes generalized and the animal remains perfectly well. Intraperitoneal inoculations of guinea pigs are equally well borne. Intravascular inoculations, performed by cardiopuncture, are perfectly well tolerated even though dosage is large. On about the fifth day following this, there appears a sudden tumefaction of the whole lymphatic system which persists about twelve days and then subsides. If animals are killed at this time they show no visceral alteration. Not a single tuberculous lesion will follow the intravascular inoculation of adult guinea pigs with as much as 100 mgm. of the bacilli. Doses of 50 to 100 mgm., introduced into the stomach through a sound and by way of the esophagus, set up a transient enlargement of the whole lymphatic system, particularly of the mesenteric nodes; but the animals remain perfectly well. Subcutaneous inoculations of rabbits are equally well borne, but the susceptibility of these animals to intravenous inoculation is much greater, for 20 mgm. frequently provokes hepatized foci of pneumonia which are crowded with bacilli and to which the animals succumb after two or three weeks. Dogs and monkeys tolerate the bacilli well. Bacilli of the forty-second subculture were still virulent, that is, tuberculogenic, for horses. Those of the two hundred and thirteenth subculture, of which 10 mgm. were given to a horse intravenously, set up a fever which lasted ten days but caused no functional trouble. The horse which received repeated large injections was killed two months after the last inoculation, when bacilli but no tubercles were found in all the viscera and lymph nodes. The horse is more susceptible to the bacilli than small laboratory animals. Massive intravenous infections provoke a febrile, typhoidal disease, which is, however, benign and unaccompanied by nodules. Repeated inoculations of the bacilli in guinea pigs, rabbits and horses disclose that the animals are made allergic by the first inoculations. Healthy animals inoculated with the bile-treated bacilli become sensitive to tuberculin. At the same time, tuberculous animals react with fever to inoculations of the bile-treated bacilli. It would appear that a single intracardiac inoculation of bile-treated bacilli confers upon guinea pigs a certain degree of increased resistance to virulent infection. On the other hand, small subcutaneous or intraperitoneal inoculations do not seem to protect against virulent infection. Experiments have not been continued long enough to determine whether the increased resistance obtained by intracardiac inoculation is durable.—*Contribution a l'étude du bacille tuberculeux bilié, A. Calmette, A. Boquet and L. Negre, Ann. d. l'Inst. Pasteur, September, 1921, xxxv, 561.*

The Avian Tubercle Bacillus.—*Certain* avian tubercle bacilli possess well-defined characters by nature which make them perfectly autonomous and do not permit of their being assimilated with the bacillus described by Koch for man and for cattle. These characters are absence of unifying substances, constancy of reaction of culture media, longevity upon artificial media opposed to feebleness of virulence, moderate ability to cause local caseation, intense toxicity for the horse, feebleness of local and general effects of tuberculin obtained from the bacilli upon tuberculous animals, and absence of specific immunizing power against human and bovine bacilli. Two of these properties in particular separate these strains from those of mammalian bacilli: these are the necrotic and immunity reactions. Avian tuberculosis arises from several causes, in which figure (1) *very exceptionally* mammalian tubercle bacilli and (2) *very frequently* acid-fast bacilli which are occasionally endowed with a certain tuberculogenic power. So far as the last named property is concerned, it occurs as irregularly and imperfectly in the second group of microörganisms as it is constant and complete in the first group and will not justify the identification of the two groups. The two types of bacilli are sometimes distinguishable absolutely by their immunity reactions.—*Recherches sur le bacille de la tuberculose aviaire, A. Jousset, Ann. d. l'Inst. Pasteur, September, 1921, xxxv, 603.*

Isolation of Tubercle Bacilli from Sputum by Petroff's Method.—Success with Petroff's method is reported. Contaminations were rarely encountered, the one which did most frequently occur being a protein-liquefying, brick-red coccus. On the average two tubes out of five gave positive cultures, growth occurring in twelve to fourteen days, when the bacilli were very numerous. The necessity of complete removal of mucus by alkali is emphasized.—*L'isolement des bacilles de Koch a partir des crachats tuberculeux d'après la méthode de Pétrof, H. Limousin, Ann. d. l'Inst. Pasteur, August, 1921, xxxv, 558.*

Tuberculosis Immune Milk.—The general subject of the transfer of immunity to various infectious and toxic substances by milk, and from mother to offspring, is reviewed and tabulated, leading to a survey of the same fields in tuberculosis. Some of the aspects of this subject studied by Maragliano and his pupils are repeated with slight experimental modifications. For immunizing, the preparations of Maragliano, *Polpa bacillare* and *Liquido F* and Deycke and Much's *MTbR*, while for antigen test reagents in complement fixation test the *antigene* and *anticorpo* of Maragliano and the partial antigens A, Fl and N were used. The milk serum and blood serum of the parent, and the blood serum of the offspring were tested for evidences of humoral immune substances, and both parent and offspring were also studied by intracutaneous injections for hypersensitiveness to the above antigens. In some human cases the umbilical cord, placenta and amniotic fluid were also examined. The studies carried out on cows and human beings indicate the transfer of antibodies and antigens from parent to foetus by the placental circulation in man, although the question still remains an open one in cattle. Antigens and antibodies are definitely transferred to the milk in large amounts in actively immunized women and cows. This transfer is not one in which the mammary glands play a passive rôle; but there results an active formation of antibodies (partial antibodies) by the receptor apparatus of the glands. The evidence seems to indicate that the calf obtains, in homologous nursing, antigens and antibodies, so that both active and passive immunization occurs, as is indicated by the presence of partial antibodies in the serum and the presence of a positive intracutaneous test during the first month after birth. The absence of a positive intracutaneous reaction in nursing infants is viewed rather as being due to a lack of proper testing methods at this age to determine hypersensitiveness. It remains to determine by further experiments on cows and man how long the immunity conferred by the placental circulation and by the milk is retained and how massive an infection this method will protect against. It is believed that the method is serviceable clinically, to prevent or markedly diminish the danger to infants and calves from infection during the first few months of life. Immune wet nurses are recommended as a further measure.—*Tuberkulose Immunmilch, A. Strubell and Theodora Strubell, Beitr. z. Klin. d. Tuberk., November 25, 1920, xlv, 38.*

Case of Spontaneous Pneumothorax in an Infant.—The onset in this case of an infant eight months old was very acute, with signs of bronchopneumonia in the left lower lobe. Eleven days after onset, pneumothorax, with collapse of the left lung, was diagnosed. This was considered to have developed overnight. Ten days later there was a considerable collection of liquid in the left pleural cavity, the diagnosis being confirmed by puncture and by X-ray. Amphoric breathing and metallic tinkle could not be demonstrated. Five months after the onset, the patient died of a supervening dysenteric enteritis. Autopsy revealed a tuberculous process, with the formation of a large cavity in the left lower lobe, and tuberculous fibrinous pleurisy. The left upper lobe and the entire right lung were free from tuberculosis.—*Sopra un caso di pneumotorace spontaneo in un bambino di 8 mesi, E. Schoenstein., La Pediatria, June 15, 1921, xxix, 535.*

Paratuberculous Pulmonary Disease.—Paratuberculous diseases of the lungs are massive infiltrations, mostly in the left upper lobe at the site of the involved lymph nodes, occurring in children of one to one and one-half years with a tuberculous infection but without constitutional symptoms. They are characterized by intense dulness, feeble or distant bronchial breathing, intense homogeneous X-ray shadows extending to the apex, a slight sensitiveness to tuberculin, and persistence for several months and resolution provided carnification does not develop. In contradistinction to chronic indurative pneumonia, long persisting paratuberculous infections do not cause contraction. Their origin is probably toxic. In 6 cases the disease was found on the side of the involved nodes and in 3 of these the findings were confirmed postmortem. Lymphatic stasis due to node involvement may account for this peculiar disease.—*Über paratuberkulose Lungenerkrankungen, S. Engel, Berl. klin. Wchnschr., August 1, 1921, lviii, 877.*

Pulmonary Tuberculosis in Cases of Surgical Tuberculous Lesions.—In a very large majority of cases an attentive examination will reveal the presence of pulmonary lesions in different phases of evolution in cases of surgical tuberculosis, and statistics show that the lung process precedes the surgical lesions. But although pulmonary tuberculosis during lymph node, bone, or joint tuberculous infection is often secondary, or at least presumed to be such, it may also be the first evidence of tuberculous infection, although it is impossible to determine the initial lesion in many instances. Between these two extremes should be placed those cases in which the lung was the first organ involved, and probably such are much more common than has generally been suspected. Therefore, the question should be studied under three heads, namely, (1) pulmonary infection in cases where the lesions have remained local for a long time; (2) bone, joint, and lymph node infection in cases of pulmonary phthisis, and (3) the part played, probably important, by latent pulmonary or lymph node infections giving rise to blood infection, in the genesis of surgical tuberculosis, the etiology of which is so frequently obscure. It is generally stated in textbooks that before making a prognosis of local tuberculous lesions the patient's general health and the presence of complications in other viscera, especially the lungs, should be first considered. Phthisis darkens the prognosis of white swellings, for according to Billroth, 16 per cent of the subjects treated for this affection in his day died of pulmonary tuberculosis, while Koenig's later statistics are about the same. From the clinical viewpoint, two conditions are to be considered. The first embraces those cases in which a surgical tuberculous lesion follows a regular or even favorable evolution. Locally everything appears to be doing well, but a pulmonary lesion exists which kills the patient. In the second case the surgical lesion has caused much deformity, numerous sinuses, and marked enlargement of the lymph nodes, and tuberculous metastases occur in the lungs from the joint or bone lesion. Although tuberculous adenitis remains for a long time a local lesion the researches of Boulay and Heckel have shown that pulmonary tuberculosis often follows. Bone or joint tuberculosis seems to provoke pulmonary infection secondarily, while adenitis, especially in the neck, seems to be the normal course followed by the infection in reaching the lungs by lymphatic contiguity. According to Marfan, Boulay, and Heckel, the infection in the lymph nodes of the neck follows the cervicomediastinal lymphatic route and the lymph nodes of the mediastinum are most frequently involved when an infection of the cervical glands exists; at least, this is what occurs in children and to some extent in adults. When, for example, the case is a joint tuberculosis, an enlargement of the regional lymph nodes indicates that the bacilli have started on a general invasion of the body; they may reach the thoracic duct, and then the pulmonary circulation becomes arrested in the fine pulmonary capillaries. This mechanism is the same as that described by Calmette in the intestinal origin of tuberculosis of the lungs, and recent experimental work has shown the importance of the lymphatic system in the generalization of local tuberculous lesions. When the tuberculous lesions of lymph nodes, bone, or joints are manifestly consecutive to pulmonary tuberculosis, the clinical picture changes. In these circumstances there is generalization of the infection; the bacilli invade the organism and create visceral lesions—bones and joints included, the development of which is the result of frequent obscure factors. Trauma, however, seems to play an important part. Between primary and secondary osteoarticular manifestations there are often very marked clinical differences in respect to the aspect and evolution of the lesions. While in the former the lesions are circumscribed and slow in progress, in the latter the invasion is rapid. The invasion of the blood by leucocytes gorged with bacilli takes place either by the direct passage of the leucocytes through the pulmonary capillaries or from the presence of a tuberculous endarteritis of the pulmonary vessels. The great number of autopsies showing that pulmonary tuberculosis exists without giving rise to clinical manifestations is now a well known fact; a minute pulmonary lesion, susceptible of cicatrization may give rise to blood infection by one of the mechanisms referred to. Therefore, the pulmonary lesions are often less evident than the osteoarticular processes and are apt to be overlooked. But there are cases in which the inverse is true, namely, that the lungs become secondarily infected from a tuberculous process in the bones or joints.—*Editorial, Med. Rec., October 1, 1921, c, 594.*

Surgical Tuberculosis.—After reviewing the various actions of specific methods of therapy, 220 cases of surgical tuberculosis, 56 of them ambulant, are reported on. The observation period on these cases covered in maximum of two and one-half years and a mean of about three-fourths to one and one-half years. Nearly all cases were X-rayed before and after treatment; and weight, urine and blood picture were studied. Detailed reports are not given, but the results are summarized. The metabolism of 8 cases treated with sunlight was improved, but no striking effects were seen. Roentgen ray treatment in 54 cases revealed a good reaction in 49.5 per cent; of these, 17 were moderate cases of bone tuberculosis of the extremities, 10 of scrofulous glands of the neck, 7 spondylitis with fistulae, 6 imperforated abscesses, 6 spina ventosa, 3 rib caries, 3 skin tuberculosis, and 3 parotid fistulae. The best results were obtained in rib caries and on neck lymph nodes. Absolute healing occurred in only 10 cases (19 per cent). The remainder, after six months of the above treatment, were given specific treatment, which yielded variable results. The use of O.T., according to Pondorff, gave relatively the best results. To stimulate metabolism, organic fatty acids (especially palmitic) were injected: 61 cases (ranging from two to sixty-two years) were treated according to Pondorff's method and with palmitic acid. Of these, 19 were definitely improved roentgenologically, 17 were healed and 22 were influenced clinically although not roentgenologically. New Tuberculin Koch, Iod-Tuberkulin, Arsentuberkulin, partigens and Tuberkulin Rosenbach gave no appreciably conclusive results. Treatment with cold-blooded tubercle bacilli in 8 cases yielded no results. The formulation of a definite scheme for treating tuberculosis seems to be impossible, on account of the marked variability of each individual case occasioned by the disease. A good pharmacological knowledge is essential to treatment, that is, a negative phase occurs for three to four days following specific treatment, after which tuberculin hypersensitiveness increases from the fourth to seventh day. In the progressive cases the more powerful specifics are not desirable. Improvement in metabolism and leucocytosis may be attained with "Aolan" or organic acids, which are advantageous remedies in reinforcing specific treatment. Operative measures should be used only rarely. Conservative treatment with rest, increasing bodily resistance with suitable nutrients, stimulation of metabolism with sunlight and baths, and the therapeutic use of the roentgen ray and fresh air are the foremost therapeutic measures to be advocated in surgical tuberculosis.—*Über chirurgische Tuberkulose, E. O. Schmidt, Beitr. z. Klin. d. Tuberk., March 15, 1921, xlvii, 106.*

Nontuberculous Anorectal Fistula Resembling the Tuberculous Variety.—Nontuberculous fistula may exist in a person who presents general constitutional symptoms which resemble those of tuberculosis, and thus obscure the diagnosis of the anorectal condition, especially if the patient's system has been undermined by the absorption of materials incident to chronic suppuration or if the patient happens to be subject to frequently recurring colds, persistent cough, etc. The following two cases of nontuberculous, foreign body anorectal fistula are reported: The first patient was admitted to the hospital with a history of a pericoccygeal abscess, for which he had undergone operation three months before and the operative wound had been treated by cleansing and by gauze drainage. The wound failed to close and presented a chronic, thin, dirty gray discharge from an opening 1 cm. below the tip of the coccyx, tenderness about the rectum and lower end of the spine, and pain which prevented the patient from following his occupation. The patient was constipated, had a hacking cough, felt weak, and steadily lost weight. He had a chronic bronchitis without alveolar involvement. Local physical examination revealed a condition which led to diagnosis of tuberculous anorectal fistula. At operation there was found a thickened globular mass between the posterior wall of the rectum, coccyx and lower sacrum which proved to be a piece of gauze such as is used for drainage. The second patient complained of pain and tenderness of the inner side of the left buttock and an annoying discharge from the wound beside the anus. His complaint had begun eight or ten months before with a swelling in that region which subsided for a short time after operation and then recurred. His digestion was poor. He had persistent cough and expectoration and he was steadily losing weight. The skin at the left side of the anus was livid and indurated, raised into folds and perforated by a number of irregular openings from which granulation tissue protruded, and a few drops of seropurulent material could be squeezed out. Probing revealed undermining of the ischiorectal fossa for a distance of about 5 cm. without perforation of the rectum. Because of the unusual character of the local lesion and the suspicious general symptoms, the diagnosis was probable tuberculous anorectal fistula. At operation a globular mass the size of a large hazel nut was found which contained a ball of hair and a thick, jellylike material, and proved to be a dermoid cyst in an unusual location.—*Simple Anorectal Fistula Simulating the Tuberculous Variety; a Report of Two Cases Presenting Unusual Features, A. A. Landsman, New York M. J., October 19, 1921, cxiv, 468.*

Tuberculous Meningitis and Hereditary Syphilis.—During the past few years the authors have seen more than twenty cases of tuberculous meningitis in children with hereditary syphilis. As a rule syphilis imparts to tuberculous lesions a definite tendency to sclerosis. Fibroid phthisis is especially prone to develop in syphilitics. When bronchiectasis, fibrinous pleurisy, mediastinitis, or adenopathy occur in young subjects, a Wassermann test should be made. Whether the formation of scar tissue, so characteristic of syphilitic infection, is an important factor in supervening tuberculous meningitis, is a subject to which too little attention has been paid. Hereditary syphilis is now claimed to be an important cause of meningeal dysfunction. This, it is proper to assume, favors the implantation of tubercle bacilli as well as other germs. It was not until the authors began doing Wassermann tests on all cases of tuberculous meningitis that they began to realize the frequency of this condition in hereditary syphilis. Many cases of the latter were discovered by blood Wassermann tests alone. If the course of tuberculous meningitis is modified in hereditary syphilis, such modification is not characteristic, though the course may occasionally be so altered as to make the diagnosis doubtful for some time. In cases where both diseases are found to be present, one must be careful not to call tuberculous meningitis a "simple meningeal reaction in syphilis," and vice versa. When, in a case with a positive Wassermann test, meningeal symptoms appear, a course of antiluetic treatment should be instituted and its results will be of great help in deciding the status of the case. Antiluetic treatment should be resorted to in all cases of tuberculous meningitis, in the hope of curing an unsuspected luetic process.—*Méningite tuberculeuse et syphilis héréditaire, V. Hutinel and P. Merklen, Arch. de Méd. d. Enfants, September, 1921, xxiv, 521.*

Diagnosis of Lung Tumors.—A primary lung tumor is one of the most difficult primary lesions to recognize early. This can only be done with a fair degree of certainty. When the condition cannot be recognized definitely an exploratory thoracotomy should be performed, whenever there is a reasonable suspicion of a primary tumor of the lung. If such a lesion is present it can be removed at the time when the operative risk is at a minimum and the chances for recovery are at their height. Clinically a pleural and a hilum type of primary lung tumor are recognized. The pleural type is most amenable to surgical treatment. A reasonable suspicion of the presence of the pleural type of primary tumor is based upon the occurrence of a one-sided pleural effusion, with or without bloody fluid, in the absence of definite signs of tuberculosis. The roentgenogram of the chest taken when the pleural cavity is inflated, after removal of the fluid, is one of the best methods of demonstrating the mass in the lungs. The hilum type is not so amenable to treatment, and the most important indications of its presence are the persistence of chronic bronchitis in the absence of tuberculosis, with blood tinged sputum, and the subsequent evidence of a mediastinal mass with pressure symptoms. In these cases bronchoscopic examination is of the greatest diagnostic value. Careful study of many cases of recurrent pleurisy and chronic bronchitis will reveal that primary lung tumors are much more common than has been heretofore believed.—*The Diagnosis of Primary Lung Tumors, A. S. Blumgarten, Am. Jour. Med. Sci., September, 1921, clxii, 376.*

Clinical Observations on Hodgkin's Disease.—Because of the ancient controversy with regard to the importance of tuberculosis as an etiological factor in Hodgkin's disease, an inquiry was made into the family history of the patients. One patient reported that a cousin had tuberculous lymph nodes in the neck and another patient believed that a maternal aunt had died from pulmonary tuberculosis. Roentgen ray examination revealed evidence of tuberculosis in only one patient and this could not be confirmed clinically or microscopically. Moreover, at necropsy no evidence of tuberculosis was found in three examinations, and in only one case was it discovered during the course of the disease. The history of this patient is not included in the present study because no clinical evidence of mediastinal involvement was found. The authors do not believe that tuberculosis plays a part in producing the disease. Besides the usual treatment, which is comparable with that used in chronic tuberculosis, many patients have been treated with radium. The glands respond most satisfactorily. Treatment by the roentgen ray probably offers most in mediastinal complications, and the authors have used it in a limited number of instances with satisfaction. It results in a replacement by connective tissue and a diminution in the size of the glands. This is particularly true of glands that are still soft and have not passed into the fibrous stage. The improvement in the patient's general health and appearance is out of proportion to the effect of the treatment on the glandular masses. These facts have recently been illustrated strikingly in a patient now under treatment. Treatment should be begun even before the deeper groups of glands can be palpated and should be kept up for a long time in association with radium, which is more useful over the superficial glands.—*Clinical Observations of Hodgkin's Disease, with Special Reference to Mediastinal Involvement, W. S. Lemon and J. B. Doyle, Am. J. M. Sci., October, 1921, clxii, 516.*

Recent Methods of Treating Pulmonary Tuberculosis.—Tuberculous patients were studied during milk (Schmidt), partigen and Friedmann's vaccine treatment. There was no marked parallel between the reaction to tuberculin and to milk. The milk injections were given according to Schmidt's directions in 55 cases (25 of these were suspected of, or had inactive or active tuberculosis), starting with 0.5 cc. and increasing to 1.2 cc. (in a few cases going up to 5 cc.). The pyrexia produced by milk is not specific for tuberculosis, as all cases, including nontuberculous ones, gave a reaction. A cutaneous or intracutaneous reaction could not be produced by milk. Subcutaneous injection of 5 cc. produced an inflammatory reaction, while 0.5 to 2 cc. caused only local pain but never produced a tuberculin-like reaction. The specificity of the tuberculin reaction is indicated by the fact that a milk reaction was obtained equally well after a previous tuberculin injection or a tuberculin reaction after a previous milk injection; while the second tuberculin injection after a similar primary treatment produced no effect at all. In cases having occasional subfebrile temperatures a progressive aggravation with increased temperature was obtained after 0.5 to 2 cc. The fever reaction in the milk treatment could not be controlled as in the tuberculin treatment. Horse serum (beginning with 0.5 and reaching 2 cc. daily in as many as 100 injections) produced more favorable results, especially during cachexia in children, which was attributed not to specific action, but rather to an action on the cachexia. The improvement was phenomenal within a few weeks. The treatment is only suitable for children in whom it produces no anaphylaxis; for this reason it cannot be used in adults. Partigens were used for diagnosis of immunity and for treatment. Judgment of the intensity of the reaction in 15 cases was difficult, on account of the difference in reaction obtained in different parts of the body. The skin reaction to partigens is no index of the immunity of the different organs or cell complexes of the body to tuberculosis. In a study of 150 cases, injected in the same part of the skin, the variations at different times were so great that no diagnostic or prognostic conclusions could be drawn. It frequently occurred that where an increase in titre might be expected the reverse was obtained. Healthy persons and patients of good resistance usually show a high intracutaneous titre to partigens. Clinical improvement is often associated with increase in intracutaneous titre. MTbR is a useful preparation for treatment, but has no visible advantages over previous forms of tuberculin treatment. In 30 cases favorable results were obtained. It is indicated in moderately severe cases where a focal reaction is to be avoided. Friedmann's vaccine was used in 63 cases, observed from seven weeks to twenty-two months. In the majority of the cases a focal reaction was not obtained. In one-half of the cases the local focus (site of injection) ruptured and later healed. No relation was noted between the course of the disease and the reaction at the local site of injection. Disappearance of toxic symptoms during the weeks following the injections was not observed. Nine cases were injected for prophylaxis and a year later the lungs were normal. Even stage II and III cases which made a good clinical impression during treatment died within six to eight months. Friedmann's vaccine is no remedy for tuberculosis, since it failed to produce results even in early cases and those with a good prognosis.—*Über einige neuere Behandlungsmethoden bei Lungentuberkulose, F. Klemperer, Berl. klin. Wchnschr., November 8 and 15, 1920, lvii, 1065 and 1095.*

Alpine Health Resorts for Tuberculous Patients.—Many indications and contraindications for curing in high altitudes are considered. Best results are obtained in the earlier cases which still manifest resistance. In toxemia and high fever cases, the body does not react so well. Cases with large multiple cavities are not suitable nor are those with a tendency to massive hemorrhages. Those with a tendency to frequent but small hemoptyses will react. Complicating chronic bronchitis is not a contraindication. Bronchial asthma is almost always helped, except in cases with marked emphysema and bronchitis. Laryngeal tuberculosis, if not too far advanced, is benefited. Pulmonary cases with decompensated hearts should not be allowed in high altitudes. Most of the cases of anemia are bettered. Rheumatic tendencies are not contraindications. Favorable results are obtained in fatigued and neurasthenic patients.—*Alpine Health Resorts for Tuberculous Subjects, B. Hudson, Brit. Jour. Tuberc., 1919, xiii, 141.*

Pütter's System of Caring for Those with Pulmonary Tuberculosis.—This system of stations in which patients with pulmonary tuberculosis are cared for has been in use in Germany for twenty years. A station comprises a director, a physician skilled in pulmonary diseases, and a nursing sister. No research is attempted in these stations, but only the practical care of patients. Various advantages of this system are enumerated, and recommendation is made that instead of the lung specialist rather a layman, trained in this particular line of work, should direct these stations.—*Das System Pütter, P. Hesse, Ztschr. f. Tuberk., April 20, 1920, xxxii, 8.*

Oxygen or Carbon Dioxide for Initial Artificial Pneumothorax.—In order to determine whether oxygen or carbon dioxide gas is best suited for preventing gas emboli, a study was made of the absorption of these gases in citrated pig blood and water. Amounts of 50 to 60 cc. in an apparatus specially devised for this purpose were used, the time allowed being $\frac{1}{4}$ to $2\frac{1}{4}$ minutes at room temperature. In $\frac{1}{4}$ minute water absorbed 19.6 cc. of a total 27 cc. of carbon dioxide, but no air or oxygen. Oxygen-rich blood absorbed, in $1\frac{1}{2}$ minutes, 0.8 cc. oxygen and 17.8 cc. carbon dioxide of 27 cc. Oxygen-poor blood absorbed, in $1\frac{1}{2}$ minutes, 1.3 cc. oxygen. Carbon dioxide-rich blood absorbed, in $2\frac{1}{4}$ minutes, 19.2 cc. carbon dioxide of 27 cc., and in $\frac{1}{4}$ minute 10.5 cc. Small amounts of carbon dioxide could not produce gas emboli on account of its rapid absorption by the blood, and it is to be preferred to oxygen or air in the primary institution of artificial pneumothorax for this reason.—*Ist Sauerstoff oder Kohlensäure zur Erstanlegung des künstlichen Pneumothorax geeigneter? Versuche über die Schnelligkeit der Absorption von Sauerstoff und Kohlensäure im Blut, H. Grass, Beitr. z. klin. d. Tuberk., March 15, 1921, xlvii, 160.*

Investigation of the Pleural Cavity in Artificial Pneumothorax.—Burnand maintains that much information regarding the condition of the pleura, whether adhesions are present or not, can be obtained from the skilful use of the needle and obturator, even when the manometer fails to show the looked for fluctuations. While recognizing the importance of the manometer, he believes that evidence given by the needle is neglected, and discusses various signs which point to free or adherent pleura and which are useful in deciding whether it is possible to produce a successful pneumothorax or not.—*Note sur la recherche de l'espade pleural dans le pneumothorax artificiel, M. R. Burnand, Rev. méd. d. l. Suisse Rom., March, 1921, xli, 148.*

Contraindications to the Administration of Artificial Pneumothorax.—Two cases are reported in which pneumothorax was administered with fatal results due to heart failure. The fatalities are attributed by the author to a combination of age (both patients were fifty years old), emphysema and rigidity of the thoracic wall.—*Eine Kontraindikation für Anlegung des künstlichen Pneumothorax, E. Rautenberg, Ztschr. f. Tuberk., April 20, 1920, xxxii, 13.*

Light Treatment of Tuberculosis.—Sunlight and artificial light therapy has been carried out for six years by the author. Twelve cases are taken up in detail (pulmonary, laryngeal, lymph node, bone and skin tuberculosis) with extraordinary results. These are illustrated with photographs and mentioned only as demonstrations of the results with light. The cases that did not respond were those in poor general condition with poor reacting powers.—*Bericht über einige mit Lichtbad behandelte Tuberkulosefälle, v. Malmström, Svenska Läkartiduingen, 1920, no. 15, 329.*

Light Treatment of Pulmonary and Laryngeal Tuberculosis.—Since 1914 patients have been treated in the Silkeborg Sanatorium, Denmark, in most cases with the mercury quartz light and only in a few cases with the carbon arc. Radiations were general, with daily exposures of ten to sixty minutes. There were no harmful results, but in a few cases it was necessary to discontinue these radiations because of fever, bronchitis, pleurisy and even erysipelas. The exposed patients were only those who were otherwise uninfluenced by ordinary routine. One hundred and thirty-three patients with pulmonary disease were treated with the quartz light; 80 were favorably influenced, 38 not influenced and 15 became worse. In 25 of 79 cases with bacilli, the sputum became bacilli-free. Twenty-five of 46 fever patients became afebrile. The general condition was bettered, as well as the appetite. Cases of pleurisy were favorably influenced. Of 22 cases of tuberculosis of the larynx, 6 were healed, 8 improved, 5 unchanged and 3 progressed. The conclusion was that light treatment in these forms of tuberculosis was a favorable aid.—*Die Lichtbehandlung der Lungen- und Larynxtuberkulose, Begtrup-Hansen, Nordisk Bibliothek for Terapi, 1920, ii, 7.*

Theory and Practice of Light Treatment of Tuberculosis.—Pigment is a collector of ray energy and transforms it into chemical energy. There may be a system of autonomic glands in connection with the skin which may give off an internal secretion. Through raying, their activity and the catalytic processes of the skin are increased. By this means substances are found which have a healing effect on the body. Comparison is made with the internal secretion given off by the adrenal glands where, in Addison's disease when these glands functionate poorly, the skin tries to compensate and as a result forms pigment. The quartz lamp should not be overestimated because it has an overabundance of short waves which are absent from sunlight. Problems are mentioned which must be worked out before a further understanding of the healing effect of light is had. Sunlight treatment is particularly recommended for it's energy-producing ability. On the ground of physical and chemical studies the action of light rays upon the body is commended.—*Zur Theorie und Praxis der Strahlenbehandlung der Tuberkulose, v. Schrötter, Strahlentherapie, 1920, xi, 605.*

Light Treatment of Bone and Joint Tuberculosis.—Sunlight treatment together with hyperemia is highly recommended. This can be applied in the lowlands as well as in the highlands. Artificial sunlight can be employed but the lamp must be such as to produce sufficient warmth. The writer emphasizes warmth as much more important than the chemical rays, and slowly increasing doses are employed. Tuberculin can also aid the treatment.—*Die Lichtbehandlung der Knochen- und Gelenktuberkulose, O. Kisch, Zeitschr. f. ärztl. Fortbild., 1920, no. 11.*

Heliotherapy in Surgical Tuberculosis.—Heliotherapy is only valuable as an adjuvant in the treatment of surgical tuberculosis together with rest, fresh air, diet, X-rays and vaccine treatment. Not all forms heal even with these. We must individualize. The bactericidal effect and the ability to produce inflammatory reactions are important. Development of a pigment is protective. It may also change the short waves to longer ones and thereby allow deep penetration. Pigment may be a measurement of ability to react. Sunlight treatment is especially valuable for abscesses and fistulae. It hastens the expulsion of sequestra and the return of motion to ankylosed joints. It should not be employed in patients who cannot pigment, in amyloid diseases and in acute, septic cases.—*The Rôle of Heliotherapy in Surgical Tuberculosis, H. Gauvain, Tubercle, 1920, i, 401.*

Heliotherapy of Surgical Tuberculosis and Necessity of Community Sanatoria for Such Patients.—Sunlight in high altitudes gives better results than that in the lowlands. It is quantitatively and qualitatively more favorable. The healing factors of high altitudes, namely, lessened barometric pressure, dryness, and freedom from dust are also important. Operative measures are also to be employed at times, namely, punctures, elimination of sequestra, and cleansing of abscesses of the soft parts. The quartz lamp is also advised where sunlight is absent. For surgical tuberculosis, community sanatoria should be built in high altitudes. There, operating-rooms with X-ray and orthopedic and mechanical appliances, which so often are lacking in sanatoria for pulmonary disease should be added.—*Einiges über die Sonnenlichtbehandlung der chirurgischen Tuberkulose und über die Notwendigkeit der Erstellung von Volkssanatorien für chirurgisch Tuberkulose, O. Barnhard, Schweiz. Rundschau f. Med., 1920, no. 22.*

Surgery of Tuberculous Joints Contrasted with Heliotherapy.—Thirteen cases of joint tuberculosis in patients, aged four to thirty-eight years, were all treated with resection by Kocher's method and healed completely. Rollier's sunlight treatment requires an abundance of time and money, and because of the inability of so many patients to carry out this procedure resection is often a more advisable method of treatment. The author has had no personal experience with sunlight treatment.—*Tuberculosis of the Joints. Rollier's Heliotherapy, G. Schweizer, Surg. Gynecol. and Obstetrics, 1920, xxx, 581.*

Heliotherapy of Lupus.—Many of the author's opinions, which have been stated on various occasions, are again presented. Light does not directly affect the tuberculous foci; only the skin is influenced. Pigment is the most important result of light. It is formed in the germinal layer, where the skin absorbs the light and assimilates it to melanin. This, like an internal secretion, is given off to the blood. An internal secretion of the germinal layer may be considered the cause of the hyperemia, so that pigmentation together with hyperemia must be had before one obtains results. The best treatment of lupus is the combination of the local with general exposures.—*Aus der Sonnenlichtbehandlung des Lupus, Jesionek, Strahlentherapie, 1920, xi, 321.*

Artificial Sunlight Treatment of Pulmonary Tuberculosis.—Of 123 patients treated with the quartz light, 8 progressive patients showed no improvement. The other cases were all of favorable prognosis, so that here the curative action of the quartz light had to be proved. No harmful effects, including hemoptysis, were ever seen. In prolonged bleeding a favorable effect seemed to be observed. Subjective betterment was regularly noted, although an increase in weight rarely occurred. The exposures can affect the disease only indirectly. Hilum tuberculosis gave good results. It is best to make use of the stimulating effect of this treatment for prevention in children rather than in adults who already have tuberculosis. A direct effect upon the tubercle bacilli in the depths can not be assumed. A formation of antibodies is not proved. The results in pulmonary tuberculosis in innumerable sanatoria are widely varied.—*Was leistet die künstliche Höhensonne bei der Behandlung der Lungentuberkulose, K. Traugott, Therap. Halbmonatsh., 1920, xiii, 350.*

Artificial Sunlight Treatment of Tuberculosis in Guinea Pigs.—Applications of artificial sunlight to experimentally infected tuberculous guinea pigs did not lengthen the life of the animals in any case. The lack of response may possibly be explained by the inability of the ultraviolet rays to penetrate.—*Höhensonne und experimentelle innere Tuberkulose beim Meerschweinchen, Hase, Zeitschr. für Phys. u. Diät. Therap., 1920, ii.*

Combined X-ray and Artificial Light Treatment of Local and Pulmonary Tuberculosis.—X-ray treatment does not always offer favorable results, and mercury quartz light exposures are therefore added in periods of five to thirty minutes, front and back, and at a distance of 50 cm., employing a dosage of X-ray according to *H.*: for deep foci 10 *H.* per field exposure, and for superficial areas (without filter) 45 *H.* per field. A 4 mm. aluminum, zinc and copper filter appeared at times too dangerous, setting up severe burns. Good results were obtained in tuberculosis of the skin, glands, joints and bones, pleura and peritoneum, and urogenital tract. Lymph nodes were treated for six months. In pulmonary disease good results were obtained only in the indurative types of hilum affections and the dosage here was 5 *H.*, front and back, in two sittings, with an interval of two to three days between. Good results in laryngeal tuberculosis were obtained by using 10 *H.* every three weeks.—*Note sur la radiothérapie combinée des tuberculoses locales et des tuberculoses pulmonaires, A. Gunsett, Jour. de radiol. et d'électrol., 1920, iv, 289.*

Treatment of Laryngeal Tuberculosis.—The healing action of the carbon arc light for lupus and surgical tuberculosis is better than that of the less penetrating quartz light. One hundred cases of moderately advanced pulmonary tuberculosis, combined with disease of the larynx, were treated with general radiations of the carbon arc light, by employing three or four powerful lamps at one time. Carbon electrodes, conveying 20 amperes, were used in lamps which ordinarily carried only 6 to 8 amperes. Exposures were made daily for a quarter of an hour the first week, then one-half hour in the second week, and three-quarters of an hour in the third week, and after that one hour. In some cases healing was complete without local treatment. In others the galvanocautery curettage, lactic acid applications, or other operative procedures were employed. Silence treatment was also carried out. Out of 79 patients, 21 were completely healed, 8 almost healed, 24 showed a marked betterment, 14 only slight, and 3 no improvement. Nine hopeless cases became worse and 6 of these died. Of the healed cases, 5 later became free from their pulmonary disease without any residue in the larynx.—*Die Behandlung der Larynxtuberkulose, N. Blegvad, Arch. f. Laryngol. und Rhinol., 1920, xxxiii, 746.*

Treatment of Tuberculous Peritonitis.—Eleven cases treated by the author were healed by radiations with the quartz lamp. If the lamp is not a complete substitute for natural sunlight, nevertheless it is a most important aid which can supply much of the healing power of sunlight when the latter cannot be obtained.—*Über Therapie bei Peritonitis tuberculosa, C. Kasemayer, Inaug. Diss., Greifswald, 1919.*

The Influence of Aureol Lamp Rays on Immunity in Pulmonary Tuberculosis.—The Siemens aureol lamp is a carbon arc lamp with the carbons lengthened so as to increase the amount of ultraviolet rays. The light rays are given off chiefly from the carbon points, whereas the arc itself delivers most of the ultraviolets. The glass globe is of a special type which is permeable to the ultraviolet rays which are present in sunlight. The short ultraviolets do not penetrate. Ordinary glass would absorb too many of the ultraviolets. The infrared rays and the ultraviolets to 290 $\mu\mu$ are therefore also utilized. The author used the partial antigens of Much, including the egg-white, group A, the fatty acid lipoid, F, and the neutral fat and alcoholic growth, N. It has been shown that the weaker the concentration which brings forth the reaction in the skin, the greater is the immunity of the body. In therapeutics a fall of the titre signifies progression of disease; a rise indicates improvement. Four patients were rayed on the trunk at a distance of 75 cm. for five minutes at the start, increasing three minutes every day, up to one hour. Both front and back were exposed. Pigmentation developed in two patients. In all four patients there was an increase of the immunity to all three antigens. This result ran almost parallel to that of Müller who found that X-rays increased reactivity to the fatty acid, whereas the mercury quartz light increased it to the neutral fat, and sunlight increased it to all three. The aureol lamp acted like sunlight.—*Über den Einfluss der Aureollampenbestrahlungen auf die Immunität Lungentuberkulöser, E. Hirschmann, Strahlentherapie, May, 1920, xi, 420.*

Ultraviolet Ray Treatment of Rickets.—Eighty rachitic children, from three months to nine years of age of whom the majority were from two to four years of age, were treated. Most of them were recent cases, but many were old or already healing. Some were those that had had deformities, as well as several in whom it was necessary to avoid crippling. The clinical results were controlled by X-ray pictures. The mercury quartz light was employed. A healing action was demonstrated in most forms. It developed more quickly than with the other means of treatment and continued over two months after the cessation of exposures. The total healing period in infants covered two to four weeks; in children of one year, one to two months; in children of two to four years, two to six months; in older children, up to nine months; and in healed rickets, one to two months. Long-wave light is less efficient than short waves and the most important healing rays are those under 300 $\mu\mu$. It was demonstrated that the visible light and warm rays do not heal rickets. The younger the child the better the after-effects. One infant with very marked craniotabes was exposed four times in ten days, with the blue light for thirty minutes at a distance of 40 cm. and ten days later the skull was completely hardened. Other similar patients were helped; but in three cases the employment of the "blue film," with three months' exposure, gave no results. One child that was similarly exposed to the sun and developed a strong pigment showed no improvement. The healing of fractures, after surgical intervention, showed no changes, whether they were rayed or not, but spontaneous fractures showed rapid healing. Exposures of twenty minutes were the most desirable, employing them three times a week. The most favorable distance was from 70 to 100 cm. The blue filter should be employed only for infants, with exposures of at least thirty minutes and at a distance of 30 to 50 cm. Tetany patients were rayed very intensively daily and on both sides. Ultraviolet rays influence florid and old cases of rickets, healing rachitic bone deformities, tetany, and the sweats and nervous manifestations of such patients. It does not influence the metarachitic bone fractures, the nonrachitic diseases of the bone, nor the reconstructed or crippled bones. It influences only indirectly the growth of bone and the teething.—*Die Ultraviolettherapie der Rachitis, K. Huldschinsky, Strahlentherapie, May, 1920, xi, 435.*

Conservative Treatment of Peritoneal Tuberculosis with X-rays.—X-ray treatment is highly recommended, both alone and in combination with operation. Best results are obtained in those cases with abundant ascites. Raying should be carried out generally after the operation. Many cases not responding to operation and showing a residue are healed by terminal radiations.—*Zur konservativen Behandlung der Bauchfelltuberkulose mit Roentgenstrahlen, A. Bircher, Strahlentherapie, 1920, xi, 647.*

Action of Small Doses of X-rays.—Rabbits were rayed, some healthy and some infected with tuberculosis. The healthy animals suffered no harm from small doses of 0.01 to 1.25 S. N. The infected animals showed a more rapid and greater dissemination of the disease. If one, however, allows the animals to manifest their resistance by raying small localized areas of tuberculosis with small doses of X-rays, then the resistance against exposures is greatly increased. On this basis some patients were treated by exposing them to small doses of soft rays and an improvement was noticed.—*Untersuchung über die Wirkung kleiner Röntgendosen, H. Eiken, Ugeskrift f. Laeger, 1919, no. 48.*

Treatment of Lupus with Iodine Exposed to X-rays.—Lupus has been treated with X-rays, radium, mesothorium, quartz, diathermia and hot air, either individually or in combination. With these methods it has been improved, but rarely healed. Operative measures or exposures with concentrated arc lights have accomplished cures. Iodine after exposures to the X-ray is found to be more easily liberated. The high atomic weight which "Iodolyester" possesses allows it by means of a strong absorption of the X-ray to exercise a marked biological action upon the diseased cells. Results in eleven cases at the Elberfeld Skin Clinic were very encouraging and demonstrated the value of this treatment.—*Behandlung des Lupus mit röntgenisierten Jodsubstanzen, Bessunger, Strahlentherapie, May, 1920, xi, 345.*

X-rays in the Treatment of Tuberculous Arthritis and Osteomyelitis.—In tuberculous arthritis and osteomyelitis there is marked improvement after the first few radiations. Pain and muscle spasm disappear almost at once, a feeling of improvement and well being replace malaise and discouragement, and the night cries will disappear. The character of the discharge from the sinuses changes. At first it may be increased, but for a few days only, when it changes to a serous type and gradually diminishes in amount, frequently drying up permanently. Some of the patients started to gain weight and color immediately after the onset of the treatments.—*Roentgen Ray Therapy in Chronic Diseases of the Bones, Joints and Tendons, H. B. Philips and H. Finkelstein, New York M. J., October 19, 1921, cxiv, 448.*

Friedmann's Treatment of Tuberculosis.—Friedmann's vaccine was used in 500 ambulant cases of pulmonary tuberculosis of various stages, glandular involvement and tuberculous pleurisies. The majority of the cases showed marked improvement in physical signs and constitutional symptoms. Tuberculosis of the neck lymph nodes disappeared gradually within three to six months. Early apical pulmonary cases gave the best results. Early skin tuberculosis was healed in six weeks. In many cases an aggravation occurred a few months after the primary injection, but disappeared after the second injection.—*Zur Friedmannschen Tuberkulosebehandlung, E. Gerdeck, Berl. klin. Wchnschr., April 25, 1921, lviii, 417.*

The Friedmann Vaccine.—An exhaustive survey of the literature on the Friedmann material led to the following conclusions: Proof is wanting for Friedmann's claim that his turtle bacillus I is a modified human type tubercle bacillus greatly reduced in virulence. Other acid-fast microorganisms, admittedly not related to the tubercle bacillus, have similar growth characteristics as respects temperature. Artificial transformation has never been definitely proved. Friedmann fails to give due consideration to the difference in rapidity and luxuriance of growth between the case of the true tubercle bacillus and that of the turtle bacillus. Although most observers have failed to distinguish between acid-fast bacilli by biological tests, a few have made sharp differentiations by agglutination. The overwhelming majority of investigators have found almost no pathogenicity for Friedmann's stock strains or for the cultures obtained from abscesses produced in man by inoculation with these germs. Occasionally, tubercles are produced by inoculation, but these are to be considered foreign body tubercles. Extension from them does not take place, nor does transplantation of such affected organs into other guinea pigs lead to infection. In his own experience Lange obtained similar results as to virulence. Bacilli, agreeing in cultural characteristics with the Friedmann bacillus, were isolated from ampules of the Friedmann material. Adaptability to varying temperature, more characteristic of saprophytes than pathogens, was noted. In doses one thousand times that necessary to kill guinea pigs with true tubercle bacilli, the material was, aside from the occasional production of abscesses, nonpathogenic. The isolated cultures were likewise nonpathogenic for guinea pigs in doses of 20 mgm., a million times the lethal dose of true tubercle bacilli. Eighty mgm. was avirulent for rabbits. One mgm., subcutaneously or intraperitoneally, was harmless for mice, as was 60 mgm. for rats. The bacillus was avirulent for fowls. A tuberculin prepared from it was nontoxic for normal animals in large doses. It was active on tuberculous animals, but only in higher doses than those required with true tuberculin. The conclusion was that the Friedmann turtle bacillus stands closer to the saprophytic acid-fast organisms than to the true tubercle bacillus and is no more dangerous than the unquestionably saprophytic forms.—*Über das Friedmannsche Tuberkulose-Schutz-und-Heilmittel. L. Lange, Ztschr. f. Immunitätsforsch., August, 1921, xxxii, 229.*

Friedmann's Vaccine in Pulmonary Tuberculosis.—Twenty-two cases were treated from October, 1918, to September, 1919, and included all stages of the disease. Five were improved after treatment, 9 were uninfluenced and 8 became worse, 3 of the latter dying. The vaccine did not have any beneficial influence which could not have been derived from ordinary dietetic-hygienic methods. The treatment rather seemed in some cases to retard the favorable progress which might be expected in similar cases of pulmonary tuberculosis not treated with the vaccine.—*Erfahrungen mit dem Friedmannschen Heilmittel bei Lungentuberkulose, O. Poehlmann, Beitr. z. Klin. d. Tuberk., March, 15, 1921, xlvii, 95.*

Experiences with Friedmann's Remedy.—Friedmann's vaccine was used in 95 cases of pulmonary tuberculosis, and 59 of these were reëxamined one to two years later. An X-ray was taken in all the cases before treatment and in many at reëxamination. Five hopeless cases at the time of treatment died. In 15, aggravation and progression of the disease occurred, 21 gave dubious results and 18 improved; of the latter 8 were definitely cured.—*Erfahrungen über das Friedmann'sche Heil-und Schutzmittel, Heggeney, Berl. klin. Wchnschr., August 29, 1921, lviii, 1037.*

Correct and Incorrect Application of Friedmann's Remedy.—Failures in the use of Friedmann's vaccine are due either to error in judging the indications for adminstration or dosage, or faulty observations combined with neglect in following up treatment after two to four months in cases showing aggravation. Three cases are reported to confirm the latter assertion. Of 75 mild cases with apical catarrh, positive roentgenological findings, temperature of 38°C., and toxic symptoms, 62 were clinically cured. In the remainder of the cases, grippe and disturbances at the area of inoculation prevented good effects. Good results were obtained in several cases of tuberculosis of the prostate and vas deferens. A case of scrofulosis in a child inoculated in 1914 was well in 1920, and the glands were hardly perceptible.—*Das Friedmann'sche Mittel bei richtiger und falscher Anwendung, A. V. Barcza, Berl. klin. Wchnschr., August 29, 1921, lviii, 1038.*

Friedmann's Remedy in the Light of Ehrlich's Side Chain Theory.—A discussion of Friedmann's remedy attempts to explain its favorable action on the basis of the formation of antibodies with "multi-avid" binding properties, which may be bound by other substances and thus account for the unfavorable results obtained at times. Raying, mechanotherapy and arsenic treatment may divert the antibodies, and thus are contraindicated.—*Die Friedmann'sche Heilmittel und die Leitlinien seiner Anwendung im Lichte der Ehrlich'schen Seitenkettentheorie, I. Tranjen, Berl. klin. Wchnschr., June 6, 1921, lviii, 601.*

Experimental Immunity Effects of Friedmann's Vaccine.—Friedmann's vaccine (100 mgm. of a young culture) was inoculated subcutaneously into guinea pigs, and six weeks later the animals were infected intracutaneously with a four weeks old culture of slightly virulent human tubercle bacilli. Sixteen guinea pigs, previously inoculated, and 16 controls received doses of 0.000,1, 0.000,01, 0.000,001, and 0.000,000,1 mgm. of bacilli in 0.1 cc. of fluid. All the animals developed a fatal tuberculosis, but a distinct difference in the development of the primary tuberculous lesions of the skin was noted in the previously inoculated animals. The formation of the ulcer was either prevented or was very much retarded, the productive inflammation predominating over the necrotic processes. This degree of increased resistance is due to the antigenic effect of the Friedmann's bacilli, as the interval of six weeks between inoculation and infection and the small amount of injected albuminous material make a nonspecific action improbable.—*Experimentelle Untersuchungen über die Wirksamkeit der Schutzimpfung nach Friedmann an intracutan inficierten Meerschweinchen, G. Töppich, Berl. klin. Wchnschr., August 29, 1921, lviii, 1035.*

Krysolgan Chemotherapy. — The sodium salt of krysolgan (p.-amino-o.-aurophenolcarbolate) was injected in ten per cent solution intravenously in doses of 0.25 to 0.2 gm. in 25 cases of chronic pulmonary tuberculosis, of which 15 were complicated by tuberculous laryngitis. Of the 10 uncomplicated treated cases none was cured, 5 were noticeably improved, and 5 remained unimproved. Of the 15 cases complicated with laryngitis none was cured, 7 were noticeably improved and 8 were not improved. There are no untoward effects from the administration of the drug, except in the weaker patients, in whom it may produce symptoms which necessitate cessation of the treatment. These symptoms are rise of temperature, lassitude, pains in the limbs, drowsiness, difficulty in deglutition, sensation of a foreign body in the throat, and especially nephritis (in 3 of the cases) with from a trace of albumin to an acute hemorrhagic nephritis.—*Klinische Beiträge zur Behandlung der Tuberkulose mit "Krysolgan", H. Rickmann, Ztschr. f. Tuberk., April 20, 1920, xxxii, 16.*

Chemotherapy of Tuberculosis with Collargol and with Colloidal Copper.—Reasoning that the action of chemotherapeutic agents may be dependent upon either pharmacological or bactericidal properties of the substance in question on the one hand and immunity phenomena on the other, emphasis is laid upon three points,—increasing the general cellular power, inhibition of and partial destruction of tubercle bacilli, and a biochemical action occasioning a liberation of antigenic substances. Colloidal copper (0.0008 gm. per cc.) and collargol (1 cc. = 0.12 gm.) were given to patients. The administration of 2 cc. of colloidal copper, subcutaneously and intravenously, produced no symptoms in rabbits and guinea pigs, when given as many as 10 injections per month. Eleven patients were given intravenous injections (2 to 3 cc.), but undesirable symptoms made the subcutaneous method seem more desirable; 12 patients being given about 80 injections, which also proved unsuccessful for obtaining the desired end. The collargol experiments proved more satisfactory: 32 cases were given 100 injections of 2.2 cc. solution. The cases were grouped as (1) chronic proliferative without tissue destruction, complication, or involvement of other organs (14 cases), (2) chronic proliferative with small cavities (5 cases), (3) chronic proliferative with pronounced cavitation (9 cases) and (4) extreme chronic cavernous phthisis with larynx and intestinal, etc., complications (4 cases). In 3 cases of (1) the injections favorably influenced the clinical picture; in 8 cases (6 (1) and 2 (2)) they led to an increase of fever and general symptomatology, but to lasting clinical benefit; in 6 cases (2 (1), 1 (2) and 3 (3)) to an increase in fever and general symptomatology without lasting clinical benefit; in 8 cases (2 (1), 1 (2), 4 (3) and 3 (4)) the temperature was reduced but the general condition was not influenced favorably; and in 7 cases (1 (1), 1 (2), 2 (3) and 3 (4)) the injections did not affect the temperature curve or general well being of the patient. Collargol therapy is considered a valuable addition in treating cases of the chronic proliferative type, in which sharp remissions or intermissions in temperature indicate severe septic conditions.—*Beitrag zur Chemotherapie der Tuberkulose. Versuche mit Collargol und kolloidalem Kupfer, H. V. Hayek Beitr. z. Klin. d. Tuberk., November 25, 1920, xlv, 17.*

Rôle of Medical Profession in Prevention of Tuberculosis.—A periodic state census which would classify all persons by means of the Pirquet test into those with open tuberculosis, those with latent infection, and those as yet free from infection, would seem to be a practical procedure. From this might follow the segregation of the first group, not only temporarily in sanatoriums, but later also in industrial systems where remunerative work would be adapted to subnormal men. The two remaining groups should be as far as possible under medical observation, particularly those with latent infection; and although the task would at first seem to be Herculean, as the sources of infection became cut off it would become less and less difficult. Periodic Pirquet examinations of children would detect the onset of infection and lead to a search for an elimination of the causes. Such a plan might be tested by an initial experiment in some selected area. Although we have come to recognize that the complete eradication of the tubercle bacillus may be an unattainable ideal, we must not relax our efforts to diminish existing foci of infection. In this respect education of both laity and physicians is of great importance and requires more and better organization, even though much has already been done in this direction. Medical men are in a position (1) to diminish and prevent infection, (2) to improve the resistance of the population by securing healthy surroundings, proper feeding and occupations, and (3) to promote the hygienic education of the masses in order to obtain their coöperation in these essentials. In the prevention of tuberculosis, medical men play their part in the following capacities: 1. As individual workers in ordinary practice, and special branches of research, and as teachers of medical students. Exerting an individual influence in his care of a certain number of people whose life history and physical condition he knows as no one else can, a medical man is the first line of defense against all forms of disease which play so large a contributory part in the clinical development of tuberculosis. The medical attendant is peculiarly well placed to supervise the general hygiene of the house and its occupants and thus exert an effect on tuberculosis, which is largely a home-bred disease. It is within his province to detect the earliest and intangible signs of failure of health from any cause, to advise as to the need for change of scene, habits, occupation, etc., to keep in close touch with health and child welfare work, and to make early diagnosis and notification of the disease. The individual worker and student of the various clinical, pathological and epidemiological aspects of tuberculosis are elements of the greatest importance in preventive work and deserve all possible support, monetary as well as moral. Physicians attached to teaching hospitals have a great responsibility, as they mold the outlook of the future general practitioner in regard to tuberculosis. There are, however, some points on which improvement is desirable. With the activity of special hospitals at which students rarely attend, and at tuberculosis dispensaries, with the natural reluctance of general hospitals to block their beds with cases of tuberculosis, there is a growing danger that full instruction in one of the commonest diseases will not be commensurate with its importance. The need for the creation of university chairs in tuberculosis is often manifested, but the supply falls far short of the demand. 2. As medical officers of state and other organizations for the prevention of disease in general and of tuberculosis in particular, medical men can play an important part in the prevention of tuberculosis. 3. As members, leaders and advisers of the general public and of municipal and other bodies, particularly the National Association for the Prevention of Tuberculosis, medical men take an active share in combating tuberculosis. They can contribute in the forwarding of all schemes for the improvement of the national well-being, which is the most efficacious means of fighting the infection.—*The Rôle of the Medical Profession in the Prevention of Tuberculosis, H. Rolleston, Internat. Jour. Pub. Health, September–October, 1921, ii, 465.*

Framingham Demonstration and Industrial Medicine.—An important phase of the Framingham Demonstration has comprised its industrial relationships and contacts. There are approximately 5,000 industrial workers in Framingham, of which about one-half are employed in a single plant which manufactures paper articles, while carpet manufacturing, boiler construction, foundries, and the manufacture of shoes and automobile bodies make up the other industries. The Demonstration has attempted a thorough survey of the industrial hazards of the community and has tried to encourage the local industries to provide adequate medical, nursing, clinic and dental services for their employees. When it started this work, only one nurse and one part-time safety engineer were employed by the industries of the community. At present, between 70 and 80 per cent of the industrial workers are under reasonably adequate medical, nursing and clinic supervision. The plant, which employs over one-half of all the workers of the community, now has a full-time physician and two nurses and maintains an excellent clinic and first-aid establishment. After the Demonstration, by effective case histories of persons ill with communicable diseases as found in this industry, had illustrated the importance of detecting such affections at the time of initial employment, the principle of compulsory examination of employees was approved and put through, with the support of the management and men. The latter became so impressed with its value that, largely at their request, a system of regular periodical medical examination for all employees was undertaken. The experience of the Framingham Demonstration has suggested that at least one full-time physician and two full-time nurses, and adequate clinic equipment, some provision for dental service and at least part-time arrangements for safety are required for an industrial unit of 2,500 people. The main functions of the nursing and medical staff would be (1) the routine operation of first-aid facilities in clinics, (2) the diagnosis of chronic affections with their reference to physicians of the patient's own choosing, (3) general health education, (4) general safety work, (5) general plant sanitation, (6) special class instruction in personal hygiene as related to matters of particular occupations as well as general habits of life, (7) particular medical advice for executive employees, (8) the regular medical examination of all new employees, and (9) the regular periodic reëxamination of permanent employees. Such medical and nursing facilities in industry can only be used to their full advantage if they are developed and operated in close coöperation with the labor groups concerned.—*The Framingham Health Demonstration and Industrial Medicine, D. B. Armstrong, Jour. Industr. Hyg., October, 1921, iii, 183.*

Need of Assistance for Preventoriums.—The sanatoriums for tuberculosis are reimbursed by the state and the communes for the care of patients; but no such provision exists for children admitted to the preventoriums. This defect in the law should be remedied, thereby permitting appropriations and gifts to be used solely for creating new establishments. This would not only be right but would be economically advantageous, since it would be the most effective means of diminishing the number of invalids that must later be cared for in hospitals or be otherwise assisted. The preventoriums should be included with the sanatoriums and benefit by the laws which provide for these.—*Création de préventoriums, nécessité d'assurer leur fonctionnement, Mouisset (Lyons), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 143.*

The Oeuvre Grancher.—The work of placing healthy children of tuberculous parents in families chosen by local physicians has been so convincing that branches have been rapidly forming in the departments, till there are now more than twenty which have joined themselves into a national federation. The Grancher plan is in such favor that it has lately been recommended by the Congress for the Advancement of Science and other learned societies. The movement is not limited to France. Work of the Grancher type was organized in Belgium before the war, and also in Italy. The Americans are said to have become acquainted in France with antituberculosis dispensaries of the Calmette type, and with the Grancher movement.—*L'oeuvre Grancher de preservation de l'enfance, Granjux (France), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 140.*

Preservation of Infants.—When Grancher founded his work the belief prevailed that tuberculosis of suckling children was rare and inexorably fatal. The Grancher work, consequently, was designed for children from three to thirteen years of age. We now know that tuberculosis of infants is nearly, if not quite always, contracted at the mother's breast; that if the child is separated from the mother at once it does not contract tuberculosis, and that, if separated from her after infection has occurred, it may be saved from death. The problem of saving nurslings is quite different from the problem of saving children old enough to share the ordinary diet of the families among whom they are distributed. A centre for the placing of nursing babies calls for a milk station, a visiting nurse who superintends the diet, and a regular consulting physician. Some attempts still in the experimental stage, have been made in France. These cannot be considered to have reached the same status as the Grancher work but they are, nevertheless, material for encouragement and inspiration.—*La préservation du nourrisson, L. Bernard (France), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 141.*

The Struggle against Tuberculosis in France.—A large scale campaign for the prevention of tuberculosis is of recent origin in France. Nevertheless, immense progress has been made in a few years. There has been a general federation of tuberculosis societies and a fusion with or withdrawal in favor of public organizations. There are 213 antituberculosis state dispensaries in operation and 155 in process of organization. Besides these, there are a number of dispensaries established by communes and departments. There are 69 sanatoriums, with a total of 7,075 beds, and 26 establishments with 7,006 beds for the care of lymph node and bone tuberculosis. These do not include the preventoriums for children. In addition to the public dispensaries and sanatoriums, there is the school for agricultural reëducation, the Franco-British colony of convalescents at Sillery and other organizations for the disabled. All the departmental organizations are directed by the National Committee of Defense against Tuberculosis. There are central bureaus for information, propaganda, liaison, etc. The National Committee regulates and coördinates the activities of all of France.—*L'état actuel de l'organisation de la lutte antituberculeuse en France, A. Guillon (France), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 129.*

Essentials in Tuberculosis Prophylaxis.—1. A universal movement should be organized to treat tuberculosis as a preventable disease. 2. Funds for this struggle should be provided by insurance against the disease, the only means, perhaps, by which certain and adequate resources could be procured 3. International legislation relating to germ carriers and means of avoiding infection, both human and bovine. 4. Revision of our conceptions respecting the infecting germ with a view to the discovery of a specific treatment. 5. New studies in defense reactions, human and animal, designed to throw light on the subject of immunity. 6. Establishment of national and international services for obtaining statistics. 7. International legislation against housing human beings in vile quarters with insufficient breathing space. 8. Coördination of societies for the protection of children, with leagues against alcoholism and the abuse of tobacco. 9. An international committee to prepare a program for the struggle against tuberculosis, to be made from the scientific and the social approaches. There should be many stations for providing clothing for persons and beds, and for furnishing separate beds in families where they would be a means of preventing infection. There should also be education in domestic prophylaxis adapted to the actual life as it is being lived in households containing tuberculous members, above all where there is open tuberculosis.—*Organisation de la prophylaxie de la tuberculose, A. E. y Capo (Spain), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 144.*

Present Efforts Against Tuberculosis in Catalonia.—Tuberculosis is on the increase in Catalonia and the housing problem is acute. Through a central institution at Barcelona the social organizations against tuberculosis in Catalonia have inaugurated a campaign of education in prophylaxis and the increase of facilities for the care of the tuberculous poor.—*Plan immédiate de la lutte antituberculeuse en Catalogne, L. Sayé (Spain), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 146.*

Organization of Tuberculosis Prophylaxis in Switzerland.—Owing to the great autonomy of the Swiss cantons the struggle against tuberculosis is largely a result of local initiative, but the regional leagues are grouped into a federal association for all Switzerland. A federal law under consideration expresses the usage in the most advanced cantons. It provides for the registration of all cases of tuberculosis, the disinfection of houses, the hospitalization of contagious cases, the supervision of tenement houses and schools, declaration by physicians of change of residence of patients and failure to comply with sanitary precautions, improvement of dwelling houses, etc. The law provides for appropriations to be made to all institutions engaged in the care of tuberculous persons or the prevention of tuberculosis. The Swiss leagues carry on three principal activities; namely, hospitalization of invalids, protection of children, and sanitation of dwellings. Part of their program includes efforts to abolsh alcoholism, supervision of food and the regulation of industry. There is also a movement directed toward the care of surgical tuberculosis. There are in Switzerland 106 antituberculosis dispensaries, 16 public sanatoriums with 1304 beds, and a great many hospitals which receive tuberculous patients. The beds for advanced cases are too few and there is a movement for the construction of special pavilions annexed to ordinary hospitals. Fines for spitting reach as high as 300 francs, an amount which serves as a sufficient demonstration of the dangers of this practice.—*L'organisation de la prophylaxie de la tuberculose en Suisse, Moris (Switzerland), Conférence internationale contre la tuberculose Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 156.*

Suggestions for Tuberculosis Prophylaxis in Italy.—Marine, alpine and agricultural colonies ought to be general. They would serve the double purpose of education in prophylaxis and protection of the community and the patient. To carry out suitable arrangements on an adequate scale, state aid is indispensable.—*Sur la prophylaxie antituberculeuse, P. Foa (Italy), Conférence international contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 147.*

The Struggle against Tuberculosis in Serbia.—Propaganda is almost the only means of opposition to tuberculosis in Serbia. This is carried on by means of notices in public places, cinema lectures, brochures, etc. Some of the large towns disinfect after the death of tuberculous persons. Only two small hospitals and a few dispensaries exist. The situation, always bad, has become very desperate since 1914. The mortality is about 10 for every 1000 inhabitants. Of every 100 persons 20 are tainted, and 10 in 100 are ill with tuberculosis.—*La lutte contre la tuberculose en Serbie, L. Stoyanovitch (Jugo-Slavia), Conférence international contre la tuberculose, Paris, October 17–21, 1920, Massonet Cie, Paris, 1921, p. 181.*

Antituberculosis Work in Rumania.—In spite of its small urban population, mortality from tuberculosis in Rumania is 31 to 32 per 10,000 inhabitants; in some regions it reaches 50; where the mortality is the greatest the housing conditions are the worst. There are three societies occupied with antituberculosis work. One is a national society engaged in prophylaxis, another is for the protection of children, and a third is a local and less important society. The present establishments for antituberculosis work consist of three sanatoriums, four dispensaries and two marine sanatoriums. The lack of money is very serious. There is at present a movement among the military authorities toward preventing the return to their homes of tuberculous soldiers and retaining them in insolation camps during their time of military service.—*La lutte antituberculeuse en Roumanie, Cantacuzène, (Rumania), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 163.*

Antituberculosis Work in Greece.—There is an antituberculosis dispensary and another centre for popular education at Athens. Patients with advanced tuberculosis are isolated in a vast hospital-sanatorium at Athens; patients with early tuberculosis are treated in high altitude stations on Parnassus and Pelion. There is a marine sanatorium for bone and lymph node tuberculosis at Voula, and a number of vacation colonies for pretuberculous children.—*La lutte antituberculeuse en Grèce, Cawadias (Greece), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 155.*

The Struggle against Tuberculosis in Holland.—A new law of 1919 has vested the conduct of public health matters in a woman and two men, who are to oversee all local associations and control the state subisdy which has increased from ten thousand florins in 1904 to a million florins at present. An intense effort has been made to combat the appalling increase in tuberculosis that occurred during the war, when the deaths rose from 14 per 10,000 inhabitants in 1914 to 20.25 in 1918. A decrease has already set in.—*Le combat contre la tuberculose dans les Pays-Bas, M. W. Pynappel (Holland), Conférence internationale contra la tuberculose, Paris, October 17–21, 1920, Masson et Cie, 1921, p. 180.*

The Struggle against Tuberculosis in Belgium.—Work for the prevention and cure of tuberculosis has increased greatly since the war, owing to the great increase in funds which the government supplies for this purpose. Dispensaries have increased from 26 to more than 100. Every district has its dispensary; and the program of child care and other antituberculosis measures in use in France, England and the United States is carried on in Belgium. Since the war, an antituberculosis coöperative society, with a capital of about ten million francs, has been established. Its form enables it to receive gifts and legacies and its work is the erection of sanatoriums in parts of Belgium where they are needed. The generous policy of the government and the effective work of the cooperative society seems to promise abundant resources.—*La lutte antituberculeuse en Belgique, G. Gregoire (Belgium), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 161.*

The Antituberculosis Campaign in Denmark.—Tuberculosis has decreased steadily in Denmark during the past forty years, falling from about 2 to about 1 in each thousand during the years from 1890 to 1919. A law, which took effect in 1906, introduced free compulsory disinfection; free treatment for all cases of open consumption; compulsory health certificates for nurses, midwives, teachers and pastors; compulsory declaration by teachers and physicians of all tuberculous school children; removal from service, with pension, for all civil employees and officials; compulsory health certificates for all persons employed in asylums, hospitals for the insane and for all members of families receiving children to be cared for. The state has established hospitals, sanatoriums, dispensaries and convalescent homes. Since 1897, when declaration of all deaths from tuberculosis became obligatory, the mortality curve has decreased regularly and the fall has not been accelerated by the important measures put in force since 1906. However it must be remembered that the law doubtless resulted in a greater number of notifications and that this increase has probably masked an acutal decrease in tuberculosis.—*La lutte antituberculeuse au Danemark, Madsen (Denmark), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 173.*

Tuberculosis Prophylactic Work in Norway.—A Norwegian law of 1900 made the registration and supervision of tuberculous patients obligatory. It provided for the removal to sanatoriums of all patients whose homes were for any reason unsuited to their condition. The cost was distributed in fixed proportions between the state, the district and the commune. Opposition to the law, which existed at first, has completely disappeared and it is generally desired to have its provisions extended, especially to increase the measures for the care of children and the poor. The provision of the law requiring hospitalization of invalids has produced, besides the great sanatoriums, a large number of tuberculosis homes. These, at first almost exclusively for incurables, have come to be used also for patients undergoing treatment. There are about 90 of these homes, with a total of some 2000 beds. They are departmental or communal or are privately endowed; the state has charge only of the great sanatoriums. The small houses are well adapted to isolate advanced cases. The Association of Norwegian Women, founded in 1901, and the National Association for Combating Tuberculosis, founded in 1910, have been assiduous in the work of propaganda. Much has been done by these and other private organizations. There is great need of funds, especially for establishments for the prevention and care of infantile tuberculosis. There has been a considerable decrease in mortality from phthisis in the entire population and a remarkable decrease in the large cities. In Christiania, from 1910 to 1917, the mortality fell from 3 to 1.78 per 1,000 and in Bergen from 3.1 to 1.96.—*L'oeuvre prophylactique contre la tuberculose en Norvege, N. Heitmann (Norway), Conférence internationale contre la tuberculose, Paris, October 17–21, Masson et Cie, Paris, 1921, p. 166.*

The Struggle against Tuberculosis in Sweden.—The Swedish sanitary organization is extremely decentralized. The state has long encouraged the local governments to maintain dispensaries and sanatoriums and to engage in other preventive and curative work. It has stimulated the local councils by appropriations and the councils have come to include the costs of dispensaries in their budgets. The local boards have been educated and inspired by the Swedish National League against Tuberculosis, which has been the pioneer in the work of instituting new experiments and demonstrating the practical usefulness of dispensary work. The league has been especially active in building asylums, open all the year, for children with tuberculous parents.—*La lutte antituberculeuse en Suede, Loevenhjelm (Sweden), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, p. 165.*

Antituberculosis Work in the Czecho-Slovak Army.—By a state regulation, most of the severe cases have been placed in military hospitals as near to their homes as possible. Patients probably curable are kept in military barracks chosen with reference to climatic suitability. The slightly affected tuberculous and those with latent disease are in convalescent camps at employments adapted to their condition. The treatment of men at home is limited as far as possible and in principle it is confined to men whose sputum is free from bacilli. These are registered with the civil authorities and must be examined once a month by a physician who has been given a history, directions for treatment, and other useful information.—*Organisation de la lutte contre la tuberculose dans l'armée Tchéco-Slovaque, C. Franz (Czecho-Slovakia), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 182.*

The Struggle against Tuberculosis in Poland.—During the forty years before 1914 the immense struggle against tuberculosis resulted in extraordinary improvement of conditions which had been very desperate. In Warsaw, for example, the mortality fell from 50.3 per 10,000 in 1879 to 20.7 in 1912; in Cracow it fell from 78.9 in 1900 to 67.8 in 1907; and in Posen from 24.22 in 1879 to 15.87 in 1907. The war brought the mortality in Warsaw from 20.7 in 1912 up to 78.4 in 1917, and the last half of the year it reached 100 in every 1000. A fifth of the population died of tuberculosis, 70 per cent of the deaths being of persons between ten and forty years. Since 1917 notification has been made compulsory and an active campaign of education has been carried on. A few dispensaries and colonies have been established and measures for protecting children are emphasized.—*La lutte antituberculeuse en Pologne, Kwiatkovski (Poland), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 186.*

Organization of Tuberculosis Prophylaxis in Argentina.—The resources available for use in the prevention and cure of tuberculosis in the Argentine Republic are extremely meagre. A national league, founded in 1899, has been active in educational prophylaxis, and has succeeded in procuring some slight state assistance. Such extremely inadequate facilities as exist for diagnosis and treatment are mostly due to private benefactions.—*L'organisation de la prophylaxie de la tuberculose dans la République Argentine, G. A. Alfaro and P. J. Hardoy (Argentina), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, 1921, p. 174.*

The Struggle against Tuberculosis in Chile.—Measures against tuberculosis in Chile are in the hands of two associations, a league which is occupied mainly with conducting seaside preventoriums for children and an association of women which carries on tuberculosis dispensaries.—*La lutte antituberculeuse au Chili, O. Fontecilla (Chile), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 179.*

The Struggle against Tuberculosis in Japan.—A law of 1914 was followed in 1919 by a second law which made important extensions to the provisions of the first. All cities of more than 50,000 inhabitants were obliged by the law to build sanatoriums and to hospitalize all of the tuberculous poor. When the support of a family was interned the municipality was obliged to provide for its members. Municipalities received power to demolish unhealthful dwellings and to build new ones; they can forbid the carrying on of trades and industries deemed unhealthy. The national treasury can appropriate, in case of need, sums ranging from one-sixth to one-half of the costs incurred by the cities. The law seems to be the most thoroughgoing yet promulgated. Under its operation several sanatoriums have been built during the past year. There are also in Japan a number of sanatoriums conducted by the Red Cross and by an imperial foundation for charity. Statistics for the past two years show a decrease in mortality from tuberculosis, which had been greatly increasing in Japan during the past thirty years.—*La lutte contre la tuberculose au Japon, S. Ujihara (Japan), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 177.*

Antituberculosis Work in New South Wales.—Only four antituberculosis dispensaries exist in New South Wales which has a population of three million. But for the scarcity of physicians caused by the war many more would now be in operation. The dispensaries classify cases for treatment into ambulatory patients, patients to be treated at home under dispensary supervision, sanatorium patients, curable hospital patients, and incurable hospital patients. The dispensaries also supervise arrested cases after sanatorium treatment and incurables who refuse hospital treatment.—*La lutte antituberculeuse dans la Nouvelle-Galles du Sud, D. Luke (New South Wales), Conférence internationale contre la tuberculose, Paris, October 17–21, 1920, Masson et Cie, Paris, 1921, p. 189.*

Specific Prophylaxis of Tuberculosis.—Methods have been worked out for the specific immunization of the newly born by utilizing the transmission of antibodies through the placental circulation and by the milk after prophylactic inoculation of women and cows. Inoculation should be initiated at the third month of gravidity and terminated six weeks before delivery. The milk of inoculated wet nurses or cows may protect children. The absorption of antibodies from the milk is promoted by removal of the casein. Immune milk or whey may be given subcutaneously.—*Über die specifische Bekämpfung der Tuberkulose, Leitsätze, A. Strubell, Berl. klin. Wchnschr., October 25, 1920, lvii, 1021.*

Petruschky's Prophylaxis.—The value of Petruschky's prophylactic tuberculin inunction experiments conducted in Hela are questioned.—*Bemerkungen zu dem Sanierungsversuch von Petruschky in Hela, E. Effler, Ztschr. f. Tuberk., April 20, 1920, xxxii, 11.*

Antigenic Action of Friedmann's Vaccine.—Fourteen nursing children were treated with Friedmann's vaccine and tested for specific allergy. None gave a positive cutaneous or intracutaneous tuberculin test to O.T. at different intervals. In four children with negative cutaneous or intracutaneous tests before vaccination and positive cutaneous test eight days after, the intracutaneous test was negative eight days and seven weeks later. In these cases there was no infiltration from the vaccination, but in 8 of the 10 other children it existed for some time, thus permitting, according to Friedmann, the formation of antibodies. In 9 of the latter 10 cases the intracutaneous test to O.T. (1:1,000 and 1:10,000) was negative after two weeks, and in one case a slight reddening occurred on the first day (1:1,000), disappearing completely on the second day. One child, tested two months after vaccination, was negative. Eight were tested after three months, of which 6 were negative; 2 showed a pseudoreaction disappearing after two days; and one was lost track of and was not tested. Seven months after vaccination, 9 children were again tested, and 5 were negative to 1:10,000 and 4 to 1:1,000 O.T. intracutaneously (2 gave a pseudoreaction which could be reproduced with saline solution in the same and other children).—*Über die antigene Wirkung der Friedmann-Bazillen, F. Loebenstein, Berl. klin. Wchnschr., June 6, 1921, lviii, 605.*

Râles in the Prognosis of Pulmonary Tuberculosis.—An analysis of 1,000 consecutive admissions to the Trudeau Sanatorium between 1907 and 1913 leads to the following conclusions: 1. Cases in which no râles were found, either on admission or on discharge examination, show the highest percentage of "cures." 2. Those patients who entered the institution with râles but who lost them during their stay form nearly as favorable a group as those showing no râles at any time. 3. In patients who entered the institution without râles but who developed them during treatment, the prognosis is much more grave than in either of the two above mentioned groups. 4. In spite of the greater frequency and the more common findings of the tubercle bacilli in right upper lesions as contrasted with left upper, the prognosis is considerably more favorable in the former class of patients. 5. Basal râles should not be diagnosed as nontuberculous too lightly, for in nearly 50 per cent in this series, tubercle bacilli were found in the sputum, and nearly 40 per cent of these developed apical râles during their stay in the sanatorium. 6. The prognosis among cases in which the râles were limited to one or both bases was not more grave than in those patients with râles over one or both upper lobes.—*Presence, Absence and Location of Râles in the Prognosis of Pulmonary Tuberculosis, F. B. Trudeau, J. A. M. A., October 22, 1921, lxxvii, 1326.*

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